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ENDOCRINE TUMORS
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20. 3173/2:

PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. INTRAOPERATIVE DELINEATION OF LESIONS IN THE SELLAR REGION WITH METRIZAMIDE.

Banna M, Schatz SW

(c/o Schatz) Dept. Neurosciences, McMaster Univ. Medical Centre, 1200 Main St. W., Hamilton, Ontario L8N 3Z5, Canada

AJNR; 2(5):461-464 1981

Forty consecutive patients with clinical and radiologic evidence of lesions in the sellar area underwent transsphenoidal injection of metrizamide (Amipaque). The patients were aged 6-82 yr (av, 48 yr) and included 24 males and 16 females. Pituitary adenomas were diagnosed in 33, chordoma in 1, sphenoidal sinus carcinoma in 1, metastases in 2, craniopharyngioma in 1, 'empty' sella in 1, and neurilemmoma in 1. Less than 1 ml of metrizamide, in a concentration of 190 mg I/ml was gently injected under fluoroscopy. In all cases the extent of the lesion was clearly demonstrated. In one patient presumed to have a pituitary tumor, metrizamide demonstrated 'empty' sella. In approx 50% of the cases, extravasation of some contrast medium outside the confines of the tumor occurred. The vascular system in one patient with pituitary apoplexy was outlined. Extravasation into the subarachnoid spaces occurred only from adenomas with suprasellar extension and was more profuse in recurrent tumors or with forced injection. The clivus was outlined in one patient and the carotid sheath was opacified in three. No clinical or endocrinologic abnormality occurred due specifically to metrizamide. The procedure did not interfere with the histopathologic diagnosis of the biopsy material. Intralesional injection of metrizamide was judged a better method for radiologic visualization of pituitary and parapituitary lesions during surgery than intraoperative pneumoencephalography. (3 Refs)

2. PATHOLOGICAL ASPECTS.

Robert F

Departement de Pathologie, Hopital Notre-Dame, Faculte de Medecine, Montreal, Quebec, Canada

Neurochirurgie; 27(Suppl1):61-73 1981

The macroscopic and light and electron microscopic findings for 214 patients (40 men, 174 women) with pituitary adenomas are described. The existence of the adenoma was indicated by prolactin levels in 208 patients and by immunocytochemical findings in 5. One patient died prior to surgery. Microadenomas, with a max diameter of 10 mm, were observed in 65% of the women and in 15% of the men. Enclosed adenomas of more than 10 mm accounted for 60% of those found in men and 26% of those found in women. Invasive adenomas occurred more frequently in women (4.5%) than in men (2.5%). Light microscopy showed that the prolactin adenomas were generally diffuse. Immunocytochemical examination for prolactin in tumors was positive in all of the tumors tested. In nearly 50% of the women and 33% of the men, fibrosis was observed. Microcalcifications were observed in 19% of the women and in 26% of the men. An infiltration of blood was found in 50% of the tumors. Electron microscopic examination indicated that the tumors were homogeneous with a well-developed golgi apparatus. Two case reports are presented. (41 Refs) (In FRE)

3. ABNORMAL REGULATION OF PROLACTIN SECRETION AFTER SUCCESSFUL SURGERY FOR PROLACTIN-SECRETING PITUITARY TUMOURS.

Schlechte JA, Sherman BM

(c/o Sherman), Clinical Res. Center, Univ. Iowa Hosp., Iowa City, IA, 52242

Clin Endocrinol (Oxf); 15(2):165-174 1981

Patients with prolactin-secreting pituitary tumors have a diminished prolactin (PRL) response after administration of a variety of stimulatory agents, including thyrotropin-releasing hormone (TRH), chlorpromazine (CPZ) and insulin-induced hypoglycemia. We examined responses to these agents in 67 women with PRL-secreting tumors before and after transsphenoidal surgery. Twenty-nine of the women were cured as defined by restoration of normal serum PRL concentrations and resumption of regular menses. One yr following transsphenoidal surgery, patients with normal PRL concentrations and regular menses had normal PRL responses to TRH, while the responses to CPZ and insulin hypoglycemia were not improved. The reversible impairment of PRL response to TRH reflects suppressed function of normal PRL-secreting cells, and the persistence of abnormal PRL responses to provocative stimuli after successful tumor removal may reflect some fundamental defect in the regulation of PRL secretion in patients with PRL-secreting adenomas. When growth hormone (GH) reserve after insulin hypoglycemia was represented as the mean absolute increment above the basal concentration and compared with normal subjects, women with PRL-secreting tumors had a diminished response that returned to normal after successful surgery. This reversible impairment of GH secretion is not adequately reflected by standard criteria for GH response and suggests that PRL may have a role in the regulation of GH secretion. (Author abstract) (46 Refs)

4. PROLACTINOMA. SURGICAL ASPECTS.

Hardy J, Mohr G

Departement de Chirurgie, Faculte de Medecine, Universite de Montreal, Montreal, Quebec, Canada

Neurochirurgie; 27(Suppl1):41-60 1981

The diagnosis and treatment of 355 patients (55 men, mean age of 39 yr; 300 women, mean age of 28 yr) with prolactinomas is described. The surgical technic employed is described. The classification of the prolactinomas observed in the 300 women and the presence or absence of suprasellar expansion is described. The sellar floor, dura mater, and venous sinus were intact in 97.3%, 95.6%, and 93.3% of the 300 patients, respectively. A tumor was found in 293/300 patients. The vol of the tumor was studied in relation to radiological stage and its visibility on the surface of the pituitary. In 260/300 cases, the tumor was grayish purple, in 20, milky white, and in 12, another color. Most (80%) of the tumors were soft, homogeneous, and easily detached in pieces with the curette or aspirator. Cysts or tumoral necrosis were observed in some patients. Suprasellar expansion was rare among the 300 women. The pituitary was normal in 230/300 women. Technical difficulties met during surgery are described. In 270/300 cases, the tumor was removed and verified by pathology. Postoperative complications and second interventions are described. Among the 275/300 patients in whom prolactin levels were measured during the 30 days following surgery, the prolactin levels were normal in 177. The 55 male patients with prolactinomas are described. Radiologically, 8 had Grade I sella turcica, 39 Grade II (18/39 with suprasellar expansion), and 8 Grade IV (5/8 with suprasellar expansion). The operative findings, postoperative complications, and surgical results are described for these men. Post-

operative prolactin levels were normalized in 20/55 men. (13 Refs) (In FRE)

5. RAPID CHANGES OF PROLACTINOMA VOLUME AFTER WITHDRAWAL AND REINSTITUTION OF BROMOCRIPTINE.

Thorner MO, Perryman RL, Rogol AD, Conway BP, MacLeod RM, Login IS, Morris JL

Dept. Internal Medicine, Univ. Virginia Sch. Medicine, Charlottesville, VA, 22908

J Clin Endocrinol Metab; 53(3):480-483 1981

Medical therapy of prolactinomas with bromocriptine has been demonstrated to reduce serum PRL levels to normal and also to reduce the size of such tumors. This size reduction may occur very rapidly. It is widely recognized that PRL levels rise again after withdrawal of bromocriptine therapy. We now describe the effects of drug withdrawal and reinstitution on tumor size in two young men harboring large prolactinomas. Bromocriptine had been extremely successful in lowering serum PRL levels by more than 80%, as well as reducing tumor size. After 12 mo of therapy bromocriptine was withdrawn. Within 48 hr PRL levels had started to rise, reaching 2,580 ng/ml at 13 days off therapy and 1,040 ng/ml at 4 wk off therapy in patients 1 and 2, respectively. At 13 days bitemporal hemianopsia recurred in patient 1, and this was associated with radiographic demonstration of expansion in the pituitary mass from a partially empty pituitary fossa to a large 12-mm suprasellar extension. The second patient remained asymptomatic,, but his tumor also reexpanded after withdrawal of bromocriptine. Bromocriptine (2.5 mg tid) was reinstituted in both cases and resulted in a rapid fall in serum PRL and reduction of tumor size in both patients; patient 1 had improvement in headaches at 24 hr, vision at 3 days, and restoration of visual fields to normal at 6 mo. Bromocriptine therapy is successful in reducing tumor size and lowering PRL levels with return of normal gonadal function. Patients with large prolactinomas treated with bromocriptine alone should be withdrawn from therapy very cautiously to avoid reexpansion of their tumor. (Author abstract) (18 Refs)

6. INCREASE OF BETA-ENDORPHIN IN CEREBROSPINAL FLUID AFTER REMOVAL OF ACTH-SECRETING PITUITARY ADENOMAS.

Furui T, Kageyama N, Kuwayama A, Nakao K, Fukushima M

Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan

Pain; 11(1):127-132 1981

Beta-endorphin (BEN) and met-enkephalin (MEK) were measured in cerebrospinal flu id (CSF) before and after removal of an ACTH-secreting pituitary adenoma in four patients with Cushing's disease. BEN was measured by radioimmunoassay, MEK was measured by radio-receptor assay, and ACTH in the plasma was measured by radioimmunoassay. After tumor resection, the ACTH level in plasma markedly decreased from 82.6 +-22.7 picog/ml to 16.7 +-4.1 picog/ml. The immunoreactive BEN level in CSF was significantly elevated after resection from 32.0 +-4.5 picog/ml to 61.8 +-10.7 picog/ml. In three cases, MEK-like substance level in CSF decreased after tumor resection, but the alteration was not statistically significant. These results suggest the possibility that BEN participates in the analgesic effect of hypophysectomy. (29 Refs)

7. THE PROLACTINOMA IN THE MAN. PREOPERATIVE EVALUATION OF 40 PATIENTS.

Somma M, Beauregard H, Rasio E

Service d'Endocrinologie, Hopital Notre-Dame, Montreal, Quebec, Canada

Neurochirurgie; 27(Suppl1):37-39 1981

The clinical and biological evaluation of 40 men (15-62 yr old) with biologically and surgically proven prolactinomas is described. A decrease in libido with sexual impotency was reported in 82.5% of the patients. Headache was observed in 45% patients. Visual field disorders accompanied optic nerve atrophy in 5/9 patients. Gynecomastia was observed in 9 patients, with galactorrhea in 6/9. Infertility was certain in 5/40 patients. Morphological hypogonadism was observed in 4/40 men. Radiological study showed that 8 patients had Stage I microadenomas, 26 had an enclosed Stage II adenomas, (12/26 with suprasellar enlargement), and 6 had invasive Stage IV adenomas (5/6 with suprasellar enlargement). In the 40 patients, base level prolactinemia ranged from 30 to 70 nanog/ml. Of the seven patients with hypopituitarism, one had partial thyroid stimulating hormone and ACTH deficiency, two had ACTH deficiency, and 4 exhibited hypopituitarism. Insulin resistance was found in 22 patients. A significant increase in prolactin was observed in only one patient. Cortisol levels were normal in 21 patients and decreased in 7. Growth hormone was normal in 15 patients and decreased in 7. In response to luteinizing hormone releasing hormone stimulation, follicle stimulating hormone was increased by greater than 100% in five patients and luteinizing hormone increased by more than 200% in six. No correlation was observed between the level of prolactinemia and patient age. The 17-beta-hydroxy-androgens were clearly decreased in the majority of the 19 patients in whom they were measured. (15 Refs) (In FRE)

8. PITUITARY METASTASIS: INCIDENCE IN CANCER PATIENTS AND CLINICAL DIFFERENTIATION FROM PITUITARY ADENOMA.

Max MB, Deck MD, Rottenberg DA

(c/o Rottenberg) Dept. Neurology, Memorial Hosp., 1275 York Ave., New York, NY, 10021

Neurology; 31(8):998-1002 1981

In order to ascertain the incidence of pituitary tumors in cancer patients and to characterize the clinical presentation of pituitary metastases, the clinical experience with these tumors at Memorial Sloan-Kettering Cancer Center during the period 1976-1979 and a recent series of 500 consecutive autopsies in which the pituitary fossa and gland had been examined were reviewed. A search was made of the English language literature for pituitary metastases; the 28 cases (reported between 1914 and 1979) which included descriptions of clinical presentation and histologic proof of metastasis were recorded. In the clinical series, 4/5 patients had symptomatic pituitary tumors; histologic diagnosis was made in three of the cases (2 adenoma, 1 metastasis). Autopsy information yielded 18/500 (3.6%) metastases and 9/500 (1.8%) adenomas; all cases had been asymptomatic pituitary tumors, and skull films performed in 15 of the patients had given no evidence of tumor. In general, radiologic evaluation did not reliably distinguish metastasis from adenoma, but the clinical syndromes were distinctive. First symptoms and signs usually point to the diagnosis. Metastases present with diabetes insipidus (DI) or less commonly with oculomotor palsies. These symptoms occur in fewer than 2% of patients with pituitary adenoma. Visual loss and anterior pituitary insufficiency, characteristic of pituitary adenoma, are infrequent initial symptoms of metastasis but may follow DI. The differentiation between pituitary metastasis and adenoma may affect therapy. (32 Refs)

9. PINEAL REGION TUMORS: COMPUTED TOMOGRAPHIC-PATHOLOGIC SPECTRUM.

Futrell NN, Osborn AG, Cheson BD
(c/o Osborn) Dept. Radiology, Univ. Utah Coll. Medicine, 50 N. Medical Drive, Salt Lake City, UT, 84132
AJNR; 2(5):415-420 1981

The heterogeneity in both histopathologic and computed tomographic (CT) appearance was demonstrated in a series of 17 pineal gland tumors, 9 of which were proven by biopsy or autopsy. Included were 4 females (av age 27 yr) and 13 males (av age 15 yr). There were two germinomas, two teratocarcinomas and one each of pineal hamartoma, benign teratoma, astrocytoma, and neurilemmoma among the biopsy-proven cases. The other cases included one 'malignant pineal tumor', one pineal lipoma, five presumed germinomas, and one undiagnosed case. A presumptive histologic diagnosis on the basis of CT alone was not possible and benign and malignant tumors could not be differentiated. An exhaustive search for a suprasellar mass is imperative in all pineal region tumors. Other lesions that should be included in the differential diagnosis of pineal tumors include exophytic brainstem glioma, neurilemmoma, incisural meningioma, intraventricular craniopharyngioma, and metastasis, since these all appear as enhancing masses in or adjacent to the posterior third ventricle or quadrigeminal plate. Since biopsy is now feasible for pineal tumors, it is recommended for treatment planning. (21 Refs)

10. MALIGNANT GERM CELL TUMOR OF THE PINEAL REGION - IMMUNOHISTOCHEMICAL STUDY OF AFP AND HCG.

Kimura N, Namiki T, Wada T
Dept. Pathology, Natl. Hosp. of Sendai, Sendai, Japan
Gan No Rinsho; 27(9):1135-1140 1981

Levels of serum and tissue alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) were determined in a 17-yr-old man with acute onset of symptoms of pineal gland tumor (endodermal sinus tumor) and in a 25-yr-old man with 6-mo duration of symptoms due to a pineal gland tumor (choriocarcinoma). The 17-yr-old patient was diagnosed on the basis of abnormal serum AFP levels (161,583.0 nanog/ml); this patient had normal serum hCG and luteinizing hormone levels. At autopsy, histological examination indicated that most of the tumor cells in the endodermal sinus tumor showed localized AFP; further study also showed that there were ip tumor implantations via a ventriculo-peritoneal shunt, metastases to mesenteric lymph nodes, and tumor cells in ascites. In case 2, a typical choriocarcinoma that was composed of syncytiotrophoblasts and cytotrophoblasts was observed; only the syncytiotrophoblastic cells were observed to contain hCG. (21 Refs) (In JPN)

11. CRANIOPHARYNGIOMAS: A CRITICAL APPROACH TO TREATMENT.

Cabezudo JM, Vaquero J, Areito E, Martinez R, De Sola RG, Bravo G
(c/o Vaquero) Servicio de Neurocirugia, Clinica Puerta de Hierro, San Martin de Porres No. 4, Madrid 35, Spain
J Neurosurg; 55(3):371-375 1981

The authors have conducted a retrospective statistical study in a series of 45 patients with craniopharyngiomas in order to assess the value of different therapeutic approaches. All the patients included in the study were placed in three groups according to their method of treatment: (1) total excision; (2) subtotal excision; and (3) surgery followed by a course of radiotherapy (RT). Symptomatic recurrence was used to define failure of treatment. Of the patients subjected to total excision, 30% experienced recurrence after a mean time of 2 yr. Tumors recurred in 71% of those treated by subtotal excision, with a mean time of 2.6 yr. Of patients receiving RT in addition to surgery, only 6% had recurrence, after a mean time of 1 yr. The authors conclude that the elective treatment for craniopharyngiomas is controlled subtotal surgery plus RT. Total excision should be attempted only if there is a negligible danger of mortality. (Author abstract) (45 Refs)

12. DIABETES INSIPIDUS AFTER SURGERY FOR CRANIOPHARYNGIOMAS.

Shibata S, Yokoyama H, Mori K
Dept. Neurosurgery, Nagasaki Univ., Nagasaki 852, Japan
Neurol Med Chir (Tokyo); 21(6):591-594 1981

A group of seven children and a group of six adults, all of whom developed diabetes insipidus after surgery for craniopharyngiomas, were compared on the basis of pre- and postoperative hormonal function, surgical method used, postoperative period within which diabetes insipidus (DI) occurred, and clinical duration of DI. Also, levels of antidiuretic hormone (ADH) were measured in 10 of the patients, and the correspondence of these levels with methods of managing the DI was investigated. Except for the two adults that died postoperatively, no differences were observed in the periods within which the DI occurred and the durations of the DI in the two groups. ADH levels were observed to drop during the course of the DI in all of the patients, and the ADH levels were low for a long time in some of the patients even after the DI had already disappeared. Strictly controlled fluid input and early administration of pitressin were recommended to manage the DI. (14 Refs) (In JPN)

THYROID TUMORS

13. CLINICAL EVALUATION OF ULTRASONIC EXAMINATION OF THYROID TUMORS, WITH REFERENCE TO THE CORRELAION BETWEEN ULTRASONIC EXAMINATION AND HISTOLOGICAL FINDINGS.

Kishimoto S, Kitamura H, Higashitsuji H, Ushio N, Hayashi M, Takamaru M
Dept. Otorhinolaryngology, Faculty Medicine, Kyoto Univ., Sakyo-ku, Kyoto 606, Japan
Jibi Inkoka Rinsho; 74(Suppl):724-735 1981

For diagnosis of thyroid tumors, palpation, x-ray, radioisotope-scintigram and biopsy have been employed. They are, however, insufficient for determining the tumor characteristic, and cause several side effects, such as spreading tumor cells and hemorrhage. In order to obtain more accurate information about thyroid tumors without any serious side effects, we evaluated 223 patients with thyroid tumors by B-mode ultrasonography, and examined 84 of them for correlation between the results of ultrasonography and the histological findings. (i) On the basis of the presence or absence of echoes within the tumor pictures, the tumors were classified as solid, cystic or mixed type. The solid type tended to be malignant, but the cystic type tended to be benign with a few exceptions. (2) On the basis of echo structures within the tumor pictures, the tumors were classified as coarse and non-uniform or fine uniform type. The latter echo has been considered to indicate benignancy. However, in 45% of those tumors malignancy was proved histologically. (3) On the basis of a marginal echo structure between the tumor and the surrounding tissue, the tumors were classified as smooth or irregular type. The latter type tended to be malignant, but the former type tended to be benign, with a few exceptions. There were nine patients with malignant tumors, four with cysts and five with encapsulated tumors. From these findings, we conclude that the classification of ultrasonographic echoes described in (1) and (3) is valuable in determining the characteristics of thyroid tumors. (36 Refs) (In JPN)

14. THE NEEDLE BIOPSY DIAGNOSIS OF PAPILLARY THYROID CARCINOMA.

Miller JM, Hamburger JI, Kini SR
Div. Endocrinology, Henry Ford Hosp., 2799 W. Grand Blvd., Detroit, MI, 48202
Cancer; 48(4):989-993 1981

One hundred five cases of papillary thyroid carcinoma (PTC) were studied by needle biopsy and surgically confirmed in a 30-mo period. Eight yr were required to diagnose the same number of cases without the use of needle biopsies. Identification of clinically unsuspected cancer and confirmation of clinically 'possible' cancer diagnoses accounted for 30% of this change. Seventy percent was accounted for by the increase in nodules referred for evaluation. The accuracy of fine-needle biopsy (FNB) improved with experience. Positive diagnoses of PTC were made in 19 of the first 35 PTCs and in 33 of the last 35. False-negative and unsatisfactory FNBs decreased from seven in the first third of the study to zero in the last third. Large-needle biopsy (LNB), initially used to check FNB, became less necessary as experience increased. Both FNB and LNB were more specific when papillary areas were included in the biopsy procedure, and approached the specificity of surgical biopsy. The increase in identifying PTC may require modification of the therapeutic implications of this diagnosis. (Author abstract) (7 Refs)

15. PREVALENCE OF CARCINOMA IN THYROID GLANDS REMOVED IN 1102 CONSECUTIVE AUTOPSY CASES.

Yatani R, Kusano I, Itoh M, Ogawa M
Dept. Pathology, Mie Univ. Sch. Medicine, Tsu, Japan
Mie Med J; 30(3):273-277 1981

The relative prevalence of carcinomas in thyroid glands was studied in a series of glands removed from 1,102 autopsy cases. Sixty-eight unselected glands were serially sliced and studied histologically. Thyroid carcinoma was found in 27/1,102 cases (2.4%): 21 were occult and 6 were active. No sex or age influence on the prevalence of occult carcinomas was found. Of the 68 glands that were serially studied, 26.5% had occult thyroid carcinoma. There were four tumors in the 16 persons less than 50 yr old and 14 in the 52 persons over 50 yr old. Four cases had two or more primaries. Seven cancers were in the right lobe, one in the isthmus, and 10 in the left lobe. Psammoma bodies were found in one gland that also had an occult carcinoma. Twenty-four cases showed significant lymphocytic infiltration, but none of these showed an occult carcinoma. Solid cell nests were found in 52 glands, heterotopic cartilage in 15, and heterotopic thymus in 7. Fibrotic foci were seen in 28 glands. The prevalence of occult carcinomas in the Japanese was approx the same in northern, middle, and southern Japan, and in Hawaii; Japan had significantly higher figures than Canada, Poland, Colombia, and the United States. (21 Refs)

16. POST-OPERATIVE CURABILITY AND RECURRENCE OF THYROID CANCER.

Kasai N, Sakamoto A, Ogawa S, Uchida M, Watanuki T
Dept. Head and Neck Surgery, Cancer Inst. Hosp., Toshima-ku, Tokyo 170, Japan
Nippon Geka Gakkai Zasshi; 82(2):121-129 1981

For the treatment of thyroid cancer, the relationship between the operative method and prognosis was analyzed using 186 cases of well differentiated carcinoma, 35 of poorly differentiated carcinoma and 25 anaplastic carcinoma. The 5-yr and 10-yr cumulative survival rates of well differentiated carcinoma, poorly differentiated carcinoma and anaplastic carcinoma were 95.1, 89.9%, 70.0, 36.8%; and 0.0, 0.0%, respectively. The duration between the operation for the primary cancer and the development of recurrence varied in every case of well differentiated carcinoma. On the other hand, most poorly differentiated carcinomas recurred within the first 5 yr. In anaplastic carcinoma, it was hard to gain more than 2 yr. survival. In conclusion, it is necessary to perform curative surgery for well and poorly differentiated carcinoma. The combined modality including surgery, radiation and chemotherapy should be given in the case of anaplastic carcinoma. (13 Refs) (In JPN)

17. MEDULLARY CARCINOMA OF THE THYROID IN THE MULTIPLE ENDOCRINE NEOPLASIA IIA SYNDROME.

Bigner SH, Cox EB, Mendelsohn G, Baylin SB, Wells SA, Eggleston JC

Dept. Pathology, Duke Medical Center, P.O. Box 3712, Durham, NC, 27710

Am J Surg Pathol; 5(5):459-472 1981

A review of the clinical, biochemical, and morphological characteristics of 72 patients (69 of whom had undergone total thyroid resection) with familial medullary thyroid carcinoma (MTC) associated with multiple endocrine neoplasia IIA (MEN IIA) is presented. Patients were categorized into groups according to tumor size: (I) less than 0.7 cm (27 patients, 5 with C-cell hyperplasia alone), (II) 0.7-1.5 cm (19 patients), and (III) greater than 1.5 cm (26 patients). Mean ages at surgery were, respectively, 19.6, 33.7, and 32.2 yr. Incidence of regional lymph node metastases was significantly lower in Groups I (4/20) and II (4/13) than in Group III (14/17); $p = 0.0001$. Elevated postoperative calcitonin levels, indicative of residual MTC, were observed significantly less frequently in Group I and Group II patients (respectively, 6/27 and 6/15) than in Group III patients (11/15); $p = 0.005$. At mean follow-up times after surgery of 3.5 and 6.0 yr, respectively, all patients in Groups I and II were alive, whereas three Group III patients had died of metastatic MTC within 2 yr of diagnosis and three additional patients died of the same cause within an unspecified time. Histologic features of the tumors varied with diameter. All tumors from Group III patients contained amyloid, whereas 9/22 Group I tumors lacked it. The majority of tumors from Group I patients had an infiltrative configuration. Presence of mitotic figures in Group III tumors correlated directly with occurrence of distant metastases and death. Early detection of minimal MTC in MEN IIA family members offers the best chance of curing patients with this tumor. (39 Refs)

18. MULTIPLE FORMS OF HUMAN TUMOR CALCITONIN DEMONSTRATED BY DENATURING POLYACRYLAMIDE GEL ELECTROPHORESIS AND LECTIN AFFINITY CHROMATOGRAPHY.

Baylin SB, Wieman KC, O'Neil JA, Roos BA
2-127A, Oncology Center, Johns Hopkins Medical Institutions, 600 N. Wolfe St., Baltimore, MA, 21205
J Clin Endocrinol Metab; 53(3):489-497 1981

The mol wt forms of immunoreactive calcitonin in human tumors have been studied using two sodium dodecyl sulfate polyacrylamide gel electrophoretic systems. Under denaturing conditions, which produce monomer peptides, it has been possible to document further the size heterogeneity of this immunoreactivity. Small mol wt forms (native size human calcitonin of 3,600 daltons and immunoreactive peptides of 4,000-6,000 daltons) predominated in extracts of four medullary thyroid carcinomas. Smaller amounts of larger mol wt forms (8,000-22,000 daltons) were detected. In one medullary thyroid carcinoma and in an extract of small (oat) cell lung carcinoma, the higher mol wt forms predominated, with the greatest amount of immunoreactivity found in 12,000-and 10,000-dalton peptides. Evidence has been obtained that all of the tumors studied contain a component of immunoreactive calcitonin that binds to lectins immobilized on agarose. Five to 20% of the total immunoreactive material from the medullary thyroid carcinomas and from human small (oat) cell lung carcinoma bound to columns of agarose-bound Concanavalin A and/or wheat germ agglutinin. The conditions of binding and elution with specific sugars strongly suggest that this lectin-bound immunoreactive calcitonin may contain mannose and N-acetylglucosamine residues. Gel electrophoresis of the carbohydrate-eluted material showed that the lectin-bound forms comprise a portion of each of the several mol wt classes of immunoreactive calcitonin moieties identified. These studies indicate further that human tumors contain different sizes of calcitonin immunoreactivity and that the ratios among these forms may vary among different neoplasms. The fact that some calcitonin forms may contain carbohydrate moieties is another potential determinant for the heterogeneity of the circulating immunoreactive calcitonin in patients with medullary thyroid carcinoma or small (oat) cell lung cancer. (Author abstract) (40 Refs)

19. DETECTING METASTASES OF DIFFERENTIATED THYROID CARCINOMA BY A SERUM THYROGLOBULIN RADIOIMMUNOASSAY USING SENSITIVE THYROGLOBULIN ANTIBODY. PRELIMINARY RESULTS.

Bednar J, Nemec J, Pichova D, Rohling S, Holusova J
Res. Inst. Endocrinology, Prague, Czechoslovakia
Radiochem Radioanal Lett; 48(6):341-353 1981

Serum thyroglobulin (TG) was measured in 117 patients with differentiated thyroi d carcinoma and in 104 controls. A modified radioimmunoassay employing a highly specific TG antibody was used. Patients were grouped according to complete or partial thyroidectomy and presence or absence of 131I-concentrating or non-131I-concentrating metastases. Patients in whom no metastases had been detected clinically or by scanning showed a range of TG levels near control (78/84 less than 110 ug/l TG). Those with detected metastases showed enhanced TG levels (27/33 greater than 110 ug/l TG). Test results could not eliminate a significant number of false positive and negative results. Normal-appearing TG levels in non-metastatic thyroidectomized patients were possibly the result of residual TG-producing tissue that was not detectable by 131I uptake. The TG radioimmunoassay appeared to be more sensitive than scanning in detecting metastases. No definitive conclusions could be made, but the assay provided useful information which could supplement other findings. (30 Refs)

20. SERUM THYROGLOBULIN IN THYROID CANCER.

Black EG, Gimlette TM, Maisey MN, Cassoni A, Harmer CL, Oates GD, Hoffenberg R
(c/o Hoffenberg) Dept. Medicine, Univ. Birmingham, Queen Elizabeth Hosp., Edgbaston, Birmingham B15 2TH, England
Lancet; 2(8244):443-445 1981

Serum thyroglobulin (Tg) was measured in 274 patients with differentiated thyroid cancer; 266 had previous thyroidectomy, which had been followed by ablative iodine-131 in 183 cases. Neither the presence nor the titer of anti-Tg antibodies appeared to effect Tg assays. Serum Tg reflected the presence or absence of cancer in 83% of 164 patients not receiving thyroxine (T4). This concordance improved to 97.5% in 158 patients tested while receiving T4. Thirty four patients in remission were tested both on and off T4 therapy; in all these patients the Tg level when receiving T4 was less than 5 ug/l. In 19 of 21 patients with cancer T4 treatment did not suppress Tg. Serum Tg thus provides an excellent marker for the presence or absence of thyroid cancer in patients taking T4, even if anti-Tg antibodies are present. It is proposed that monitoring of patients by assay of serum Tg should supplant routine assessment by radioactive-iodine scans of the neck or whole body. (Author abstract) (14 Refs)

21. TISSUE LEVELS OF MONOAMINES AND MONOAMINE METABOLIZING ENZYMES IN MEDULLARY CARCINOMA AND OTHER THYROID DISEASES.

Feldman JM, Wells SA
Box 2963, Duke Univ. Medical Center, Durham, NC, 27710
Am J Med Sci; 282(1):34-40 1981

Medullary carcinoma of the thyroid (MCT) originates from the parafollicular cells of the thyroid. Many MCT contain large quantities of histaminase. There are some histologic and biochemical suggestions that MCT also may contain increased quantities of monoamines such as serotonin and norepinephrine (NE). This report compares the levels of monoamines and monoamine metabolizing enzymes in nine consecutive MCT removed in our medical center with the levels in normal thyroid tissue, follicular adenomas of the thyroid, colloid nodules of the thyroid, and chronic (Hashimoto's) thyroiditis tissue. There was no significant difference in the serotonin, NE, and dopamine concentrations in most MCT and normal thyroid tissues. Although the serotonin concentration of follicular adenomas and colloid nodules did not differ from that of normal thyroid tissue, the NE concentration of colloid nodules was decreased. The monoamine oxidase (MAO) and catechol-o-methyltransferase (COMT) activity of MCT and colloid nodules did not differ from normal thyroid tissue. The MAO activity of follicular adenomas was significantly higher than the MAO activity of normal thyroid tissue when the enzyme activity was expressed either per unit protein or per unit DNA. The COMT activity of follicular adenomas was significantly higher than the COMT activity of normal thyroid tissue when expressed per unit protein, but was not significantly different when expressed per unit DNA. One of the nine MCT we evaluated had increased levels of NE, dopamine, MAO and COMT. In addition, it contained increased amounts of epinephrine and the epinephrine synthesizing enzyme phenylethanolamine-N-methyltransferase. We conclude that the levels of monoamines and monoamine metabolizing enzymes are not increased in most MCT. However, the activity of MAO is increased in other neoplasms such as follicular adenoma. (Author abstract) (31 Refs)

PARATHYROID TUMORS

22. REOPERATION FOR PRIMARY HYPERPARATHYROIDISM.

McGarity WC, Goldman AL
Emory Univ. Clinic, 1365 Clifton Road, N.E., Atlanta, GA, 30322
Ann Surg; 194(2):134-139 1981

Between 1960 and April, 1980, 302 patients were explored for primary hyperparathyroidism at Emory University Hospital. Seventeen of these 302 patients had undergone initial surgical exploration elsewhere, and were referred for persistent hypercalcemia. Of the 285 patients who were operated on at our institution, 14 subsequently had persistent hypercalcemia, and 2 had recurrent hypercalcemia. Twenty-eight of these 33 patients had had re-exploration, and 23 (82%) are now normocalcemic. Twenty-eight abnormal glands were found; 22 (79%) were retrievable via the neck and 6 (21%) required sternotomy. Of those glands removed via the neck, 9 were in a near normal location and 13 in a subnormal or abnormal location. The causes of initial surgical failures were abnormally located glands, in 10 patients, insufficient explorations of the neck in 8 patients, hyperfunctioning parathyroid remnants in 3 patients, inadequate plans for hyperplasia in 2 patients, and carcinoma in 1 patient. In 57% of our patients who underwent successful re-exploration, the glands were correctly localized before operation by angiographic examination or selective venous sampling for parathormone. Thorough exploration and obtainment of biopsy specimens of all parathyroid glands are recommended in order to keep initial failures to a minimum. If reoperation is required, localization using CT scan, angiography and selective venous sampling are recommended. (Author abstract) (8 Refs)

23. PROGRESSIVE RENAL FAILURE IN SURGICALLY TREATED HYPERPARATHYROIDISM.

Dixon J, Smith JF
Dept. Pathology, John Radcliffe Hosp., Headington, Oxford, England
J Clin Pathol; 34(7):730-737 1981

Of 570 patients operated on for hyperparathyroidism, 18 subsequently died (between 1 day and 12 yr after operation). Pathological findings at necropsy in these patients have been reviewed. Four necropsies on patients with untreated hyperparathyroidism have also been reviewed for comparison. Of these 22 cases, 14 had renal failure at the time of death. This was attributed to the following: nephrocalcinosis (6); chronic glomerulonephritis (4); analgesic nephropathy (1); cystinuria (1); sarcoidosis (1); and polycystic disease (1). Of those with renal failure due to nephrocalcinosis, three had persistent hypercalcemia after operation; the other three survived only for a short time. There was no evidence of residual nephrocalcinosis producing progressive renal failure if the plasma calcium concentration was corrected. In those with chronic glomerulonephritis, cystinuria, and polycystic disease, the hyperparathyroidism was considered to be tertiary to the renal disease but renal failure was not always present at the time of diagnosis. (Author abstract) (11 Refs)

24. UNEXPECTED PARATHYROID DISEASE DISCOVERED AT THYROIDECTOMY IN IRRADIATED PATIENTS.

Prinz RA, Paloyan E, Lawrence AM, Barbato AL, Braithwaite SS, Brooks MH
Dept. Surgery, Loyola Univ. Stritch Sch. Medicine, 2160 South First Ave., Maywood, IL, 60153
Am J Surg; 142(3):355-357 1981

Eight of 23 patients undergoing total thyroidectomy for radiation-associated nodular thyroid disease were found to have unsuspected parathyroid hyperplasia or adenoma at operation. The total serum calcium level was normal preoperatively in each patient. Serum ionized calcium and parathyroid hormone levels were measured in five patients preoperatively and were normal in each case. These pathologic findings in normocalcemic patients may represent a preclinical form of hyperparathyroidism, which would be further evidence linking radiation to the pathogenesis of hyperparathyroidism. The parathyroid glands should be evaluated both preoperatively and at operation in all patients who have a history of radiation and require thyroidectomy. (Author abstract) (25 Refs)

ADRENAL TUMORS

25. THE CLINICAL INVESTIGATION OF ADRENAL ANGIOGRAPHY.

Ito T
Dept. Radiology, Sch. Medicine, Kagoshima Univ., Kagoshima, Japan
Nippon Igaku Hoshasen Gakkai Zasshi; 41(4):320-349 1981

Adrenal angiography was investigated clinically in detail with special reference to anatomical analysis of angiographic appearances, characteristics of angiographic findings on some adrenal diseases and also the diagnostic accuracy between arteriography and venography. The adrenal angiograms of 92 patients, (56 hypertension or obesity; 19 primary aldosteronism, 7 Cushing's syndrome, 2 pheochromocytoma, 2 adrenogenital syndrome, 1 each non-functioning adenoma, cyst, hemangioma, metastatic tumor and Addison's disease) were subjected to the investigation. The obtained results were as follows: (1) Forty-seven selective inferior phrenic arteriograms and 43 selective middle adrenal arteriograms in 40 patients, and 59 inferior adrenal arteriograms (right 34, left 25) in 60 patients could be visualized. From the observation of these adrenal arteriograms, it was considered that on the right adrenal gland the catheterization to the right inferior phrenic artery and the right inferior adrenal artery, and on the left adrenal gland the catheterization to the left middle adrenal artery were beneficial and favorable procedures for the purpose of visualizing the adrenal glands adequately. (2) Catheterization of adrenal vein in 90 patients was successful at the rate of 98.9% on the left side and 76.7% on the right side. (3) Nineteen patients with primary aldosteronism were studied with regard to adrenal venography, arteriography and aldosterone assay in the adrenal vein. The diagnostic accuracy was 94.1% (16/17) at venography, 71.4% (10/14) at arteriography and 92.9% (13/14) at venous aldosterone assay. (4) Seven patients with Cushing's syndrome were all diagnosed with venography, and three patients were also diagnosed correctly by arteriography. (5) Venographic differential diagnosis on hyperplasia of Cushing's syndrome, primary aldosteronism and adrenogenital syndrome were considered to be difficult. (6) Twenty-eight of 36 patients with abnormal angiographic findings were operated on and all were proved to be correctly diagnosed. Over all, the diagnostic accuracy was 96.7% (29/30) at venography, 76.0% (19/25) at arteriography and 39.1% (9/23) at abdominal aortography. (69 Refs) (In JPN)

26. FOLLOW-UP STUDY ON TREATMENT IN 27 PATIENTS WITH CUSHING'S DISEASE: ADRENALECTOMY, TRANSSPHENOIDAL ADENOMECTOMY AND MEDICAL TREATMENT.

Tomita A, Suzuki S, Hara I, Oiso Y, Mizuno S, Yogo H, Kuwayama A, Kageyama N

1st Dept. Internal Medicine, Nagoya Univ. Sch. Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan

Endocrinol Jpn; 28(2):197-205 1981

A summary of the results of treatment over a period of 18 yr of 27 patients (5 male, 22 female) with Cushing's disease is presented. Adrenalectomy was performed on 21 patients (19 total bilateral adrenalectomy, 2 unilateral adrenalectomy): 4 died of causes not directly related to the operation. Nine bilaterally adrenalectomized patients had hyperpigmentation despite cortisol replacement therapy (20-30 mg/day) and elevated plasma ACTH levels not completely suppressed by daily 2, 4, or 8 mg dexamethasone po or 2.5 mg bromocriptine. Pituitary adenomectomy by the transsphenoidal approach was performed on five patients. Three were cured but one has required postoperative cortisol replacement therapy for hypopituitarism for 1 yr to this date, and two have had a recurrence of Cushing's syndrome after 6-8 mo remissions (1 successfully treated with bromocriptine). Various medical treatments were attempted. Reserpine (1-2 mg/day for 2 yr) and cyproheptadine (24 mg/day) were ineffective and the patients so treated later underwent adrenalectomy; bromocriptine (2.5 mg/day) effectively lowered plasma ACTH, plasma cortisol, and urinary 17-hydroxycorticosteroid in 2/6 patients. The findings are compared with reports in the literature. (20 Refs)

27. EFFECTS OF VALPROIC ACID, NALOXONE AND HYDROCORTISONE IN NELSON'S SYNDROME AND CUSHING'S DISEASE.

Elias AN, Gwinup G, Valenta LJ

Div. Endocrinology, UCI Medical Center, 101 City Drive South, Orange, CA, 92668

Clin Endocrinol (Oxf); 15(2):151-154 1981

Two patients with Nelson's syndrome and one patient after bilateral adrenalectomy for Cushing's disease, without any evidence of Nelson's syndrome, were studied with respect to the effect of hydrocortisone, naloxone and valproic acid (a GABA transaminase inhibitor) on ACTH secretion. Hydrocortisone suppressed plasma ACTH concentrations to normal in the patient without Nelson's syndrome, but failed to do so in the two patients with Nelson's syndrome. Naloxone and valproic acid caused a decline in plasma ACTH concentrations in the patients with Nelson's syndrome, but produced no change in the patient without Nelson's syndrome. Secretion of ACTH may thus be influenced by both opiate peptides and by gamma aminobutyric acid, as well as by the cortisol concentrations, these agents may act a different sites to inhibit ACTH release by the tumor. (Author abstract) (14 Refs)

28. MALIGNANCY ASSOCIATED WITH CONGENITAL ADRENAL HYPERPLASIA.

Duck SC

(c/o) Pediatric Endocrinology, 1700 W. Wisconsin Ave., Milwaukee, WI, 53233

J Pediatr; 99(3):423-424 1981

Four patients with 21-hydroxylase deficiency adrenal hyperplasia (HDAH) who developed a malignant tumor are described. These patients were among 42 children from 36 families diagnosed as having HDAH. The diagnosis of HDAH was based on both elevated 17-ketosteroid and pregnanetriol levels and depressed 17-hydroxycorticosteroid levels. By the time of diagnosis the perirectal malignancy, proven by biopsy in Patient 1, had metastasized to the lungs. The patient died within 2.5 mo. The other three patients were thriving at the time of report: Patient 2 was disease free; Patient 3 underwent repeated spinal surgery for tumor regrowth in 1979 and continues to grow along the 25th to 50th percentiles; Patient 4 was responding appropriately after 14-18 scheduled mo of chemotherapy. Patient 3 also had juvenile schizophrenia and trisomy of the proximal segment of the long arm of chromosome 13. The coexistence of neoplasms in children with HDAH is discussed. (9 Refs)

29. MULTIPLE PLASMA STEROID RESPONSES TO GRADED ACTH INFUSIONS IN PATIENTS WITH PRIMARY ALDOSTERONISM.

Guthrie GP

Div. Endocrinology, Dept. Medicine, Univ. Kentucky Coll. Medicine, Lexington, KY, 40536

J Lab Clin Med; 98(3):364-373 1981

We measured the simultaneous responses of eight plasma steroids to the infusion of alpha 1-24 ACTH at incremental rates of 12.5 to 200 mIU/30 min in seven patients with primary aldosteronism (5 with adenomas, 2 with adrenal hyperplasia) and in 10 normal controls studied on regular sodium intakes and while supine. Patients with primary aldosteronism from adenomas had relatively higher concentrations (p less than 0.05) of aldosterone, 18 OH-B, corticosterone, and DOC than the two with hyperplasia and, save corticosterone, above the range of the normal controls. We found inconsistent differences in plasma progesterone, 17-hydroxyprogesterone, deoxycortisol, and cortisol. These findings suggest that the intermediate steps in aldosterone biosynthesis are hypersensitive to physiologic amounts of ACTH in patients with aldosterone-producing adenomas. Plasma levels of steroids distal to progesterone, ie, DOC, corticosterone, 18 OH-B, and aldosterone, are relatively higher after small amounts of ACTH in patients with adenomas than in normal subjects or those with adrenal hyperplasia. (Author abstract) (29 Refs)

PANCREAS TUMORS

30. THE DIFFERENTIAL DIAGNOSIS OF THE PANCREAS DISEASES WITH THE COMPUTERIZED TOMOGRAPHY.

Castrup W, Herrmann R
Radiologische Klinik, Kreiskrankenhaus, Schwarzenmoorstr. 70, 4900 Herford, W. Germany
Dtsch Med Wochenschr; 106(34):1072-1076 1981

The computerized tomography has improved and refined the diagnosis of the diseases of the epigastrium organs. The pancreas (P) size, shape, tissue structure and the surrounding tissue layers, especially peripancreatic fat, neighboring blood vessels and fibrous tissues. The oral intake of larger doses of diluted contrast agents can clearly delineate the stomach and intestines and by injecting the contrast agents the same can be done with the blood vessels. Generally pancreatitis and cancer will increase P size. The density of the normal P tissue is between that of the liver, which is the highest and the kidney. The CT cannot distinguish the tumor tissue from the normal parenchyma, but in some cases of the resected P tumor the density. was somewhat higher and the density deviation lower. This was not confermed in vivo yet. In some cases especially in the large, inoperable tumors there are areas of lower density due to necrosis or cystic degeneration. The rare cystic adenomas show in CT cystic areas undistinguishable from the pseudocysts of the chronic pancreatitis, but can be recognized by their pronounced hypervascularization and collateral structures. The insulinomas can be recognized by their high density even when their diameter is only 1-2 cm. The P cysts appear also in polycystic degeneration of the kidneys or liver. In such cases Ct can show clearly all the epigastrium organs in a few sections. (32 Refs) (In GER)

31. DIMETHYLTRIAZENOIMIDAZOLE CARBOXAMIDE THERAPY OF ISLET CELL CARCINOMA OF THE PANCREAS.

Awrich AE, Peetz M, Fletcher WS
(c/o Fletcher) Div. Surgical Oncology, Univ. Oregon Health Sciences Center, Portland, OR, 97201
J Surg Oncol; 17(4):321-326 1981

Four patients with metastatic glucagonoma and one patient with metastatic diarrheogenic islet cell carcinoma of the pancreas were treated with dimethyltriazenoimidazole carboxamide (DTIC), 250 mg/M2 daily for 5 days repeated every 4 wk. All patients responded clinically and chemically in one or more ways by a reduction in plasma glucagon levels, improved glucose tolerance, decreased measurable tumor, wt gain, and resolution of necrolytic migratory erythema and diarrhea. This experience and other cases from the literature call for the investigation of DTIC as the initial therapy in metastatic islet cell carcinoma of the pancreas and as being of possible benefit in other tumors of neuroendocrine origin. (Author abstract) (18 Refs)

32. PROTEAN MANIFESTATIONS OF NEONATAL HYPERINSULINISM.

Mayer T, Matlak ME, Lowry SF, Gooch WM, Johnson DG
804 Poplar Ridge Drive, Chesapeake, VA, 23320
Ann Surg; 194(2):140-145 1981

Endogenous hyperinsulinism is the leading cause of persistent hypoglycemia in children under 1 yr of age. Classically, the symptoms of neonatal hypoglycemia have been referable to CNS dysfunction, with seizures described in nearly all patients. Our experience with eight neonates emphasizes the protean manifestations of this disease. One patient presented with a maternal history of diuretic use, and developed asymptomatic hyperinsulinism documented by provocative testing. The hyperinsulinism cleared after 2 wk of medical therapy. This transient hyperinsulinism may have been secondary to use of a thiazide-type diuretic. A second patient presented, as a neonate, with a large abdominal mass but no seizure activity. Exploratory laparotomy revealed an 11 x 5 x 3 cm pancreatic tumor, which required splenectomy, 60% gastrectomy and duodenectomy for removal. Histologic examination demonstrated an insulin-secreting hamartoma. A third patient died suddenly without prior symptoms, and was found to have striking nesidioblastosis on pathologic examination. One infant presented with absence of the abdominal musculature (prune belly syndrome) and features of the Beckwith-Wiedeman syndrome, as well as profound hypoglycemia. Only three patients had seizures, and an additional patient had jitteriness. Pathologic diagnoses were nesidioblastosis (n = 2), islet cell hyperplasia (n = 1), adenoma (n = 1), hamartoma (n = 1), transient hyperinsulinism (n = 1). One patient's pancreas showed areas of nesidioblastosis, islet cell hyperplasia, and a discrete adenoma in the region of the common bile duct. Careful diagnostic testing is essential in these patients, inasmuch as hypoglycemia is poorly tolerated by neonates and infants. Using the diagnostic algorithm presented here, all patients' endogenous hyperinsulinism was documented quickly and efficiently. Recognition of the broad spectrum of symptoms with which these patients may present is essential if serious neurologic sequelae are to be avoided. (Author abstract) (15 Refs)

33. IMMUNOCYTOCHEMISTRY AND ELECTRON MICROSCOPY OF AN ARGENTAFFIN ENDOCRINE TUMOUR OF THE PANCREAS.

Wilander E, El-Salhy M, Willen R, Grimelius L
Dept. Pathology, Univ. Uppsala, P.O. Box 533, S-751 22, Uppsala, Sweden
Virchows Arch [Pathol Anat]; 392(3):263-269 1981

An endocrine pancreatic tumor that had not caused any endocrine symptoms was examined by histological, immunocytochemical and electron microscopic techniques. The majority of the tumor cells were argentaffin and contained secretory granules of the enterochromaffin cell type. Immunocytochemically a minority of tumor cells reacted to antisera against beta-endorphin, met- and leu-enkephalin, gastrin, somatostatin and ACTH. The tumor was thus multihormonal, and appeared to be more closely related to the classic Carcinoid tumors of the mid-gut than to most pancreatic endocrine tumors. (Author abstract) (20 Refs)

GONADAL TUMORS

34. NEUROHORMONAL PEPTIDE IMMUNOREACTIVE CELLS IN MUCINOUS CYSTADENOMAS AND CYSTADENOCARCINOMAS OF THE OVARY.

Sporrong B, Alumets J, Clase L, Falkmer S, Hakanson R, Ljungberg O, Sundler F
(c/o Falkmer) Dept. Pathology, Univ. Lund, Malmo General Hosp., S-21401 Malmo, Sweden
Virchows Arch [Pathol Anat]; 392(3):271-280 1981

In 144 benign mucinous cystadenomas of the ovary, 33 mucinous cystadenomas of borderline malignancy and 64 mucinous cystadenocarcinomas, the incidence of tumors containing argyrophil (and probably endocrine cells) was 18%, 33%, and 53%, respectively. The results of a semiquantitative assessment of the number of argyrophil cells in each individual tumor indicates that the greatest numbers occurred in the cystadenocarcinomas. As, however, the tumor cell density was larger in the cystadenocarcinomas than in the cystadenomas, and as the argyrophil cells often had a patchy distribution in the tumor epithelium, the incidence figures are unreliable. In addition, visualization of the argyrophil cells depends on an adequate fixation which is difficult to achieve in the routine processing of large tumor specimens. Many argyrophil cells in the cystadenocarcinomas displayed immunoreactivity with antisera raised against gastro-entero-pancreatic (GEP) neurohormonal peptides. In 10 such tumors immunohistochemical evidence was obtained for the presence of the following neurohormonal peptides in the tumor cells: somatostatin, glucagon, gastrin/CCK, neurotensin, and enkephalin. Four of these 10 cystadenocarcinomas were multihormonal, in that 3 contained two cell populations storing GEP neurohormonal peptides, and 1 tumor even three such populations. In the benign cystadenomas, however, no immunoreactive tumor cells were found. In those of borderline type, only two harbored immunoreactive cells. In both cases the tumor cells stored gastrin/CCK. The general appearance of the epithelium in the mucinous tumors - a continuous single-cell layer of mucin-producing cells intermingled with argyrophil cells of open type - and the spectrum of neurohormonal peptides observed, indicate an origin from the foregut endoderm. (Author abstract) (29 Refs)

35. MALIGNANT GERM CELL TUMORS OF THE OVARY; CLINICOPATHOLOGICAL STUDY.

Ishige H, Nagao K, Kuwahara T, Ueno T, Maruyama K, Suzuki M, Shoogimen M, Yoshiwara T

Dept. Pathology, Chiba Cancer Center Res. Inst., Nitona-cho, Chiba 280, Japan

Chiba Med J; 57(1):19-28 1981

During the period from 1973 to 1979, eight patients (including four unmarried women) with malignant germ cell tumor of the ovary were treated at our clinic. By the WHO classification, these cases included one case of embryonal carcinoma, one case of dysgerminoma, two cases of endodermal sinus tumor, one case of teratoma mixed with choriocarcinoma. one case of teratoma mixed with endodermal sinus tumor and two cases of dysgerminoma mixed with endodermal sinus tumor. Clinicopathological findings of these patients were reviewed in association with the serum level of 'tumor products' including alpha-fetroprotein (AFP), human chorionic gonadotropin (HCG), carcinoembryonic antigen and lactic dehydrogenase (LDH). The age range was 15 to 43 yr (av 28 yr). The serum level of AFP was elevated in all patients with endodermal sinus tumor. The serum level of HCG was elevated in only one case of choriocarcinoma mixed with teratoma in which HCG was identified by the immunoperoxidase technique in choriocarcinoma cells. The serum level of LDH was elevated in all patients with lethal tumors. The measurement of the serum level of specific tumor products was helpful in determining the extension and recurrence of the tumors and prognosis of patients. While lymph node metastasis was seen in one case of embryonal carcinoma and visceral organ metastasis was seen in two cases of teratoma mixed with choriocarcinoma, and embryonal carcinoma, peritoneal carcinomatosis was seen in all patients, indicating the rapid growth rate of these tumors. (22 Refs) (In JPN)

36. IMPROVED HUMAN CHORIONIC GONADOTROPIN DETECTION WITH CARBOXYL-TERMINAL RADIOIMMUNOASSAY OF THE BETA SUBUNIT ON CONCENTRATED 24-HOUR URINE IN PATIENTS WITH TESTICULAR CANCER.

Javadpour N, Chen HC
Surgery Branch, NCI, NIH, Bethesda, MD, 21205
J Urol; 126(2):176-178 1981

The value of measuring serum levels of human chorionic gonadotropin in detecting and monitoring testicular cancer has been demonstrated convincingly. In this study the human chorionic gonadotropin was extracted by the kaolin-acetone procedure from 24-hr urine specimens and the total vol of the extract was adjusted to 15 ml. With a highly specific immunoassay system (H93) that recognizes the unique carboxyl-terminal peptide of human chorionic gonadotropin beta subunit (residue numbers 123 to 145) as described previously, the urinary human chorionic gonadotropin was measured serially in 32 specimens of 15 patients with initially human chorionic gonadotropin-producing testicular tumors. These 15 patients had simultaneous measurements of serum human chorionic gonadotropin using an antiserum against the beta subunit (Sb6) and urinary human chorionic gonadotropin concentrates using H93 radioimmunoassay. The initial serum hormone levels of these 15 patients were elevated and returned to normal after therapy. However, despite this occurrence the urinary hormone levels also were elevated. The initial five patients with elevated urinary but normal serum human chorionic gonadotropin levels had recurrence. The use of this highly specific radioimmunoassay in measuring urinary human chorionic gonadotropin coupled with effective chemotherapeutic agents has been valuable in selecting patients in whom further therapy is warranted despite normal serum human chorionic gonadotropin and clinically undetectable tumor. (Author abstract) (9 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

37. STUDIES ON THE INDICATORS FOR THE RESPONSIVENESS OF HUMAN BREAST CANCER TO SEX STEROIDS.

Boku S
Dept. Obstetrics and Gynecology, Kyoto Prefectural Univ. Medicine, Kyoto 602, Japan
Nippon Naibunpi Gakkai Zasshi; 57(1):64-88 1981

Characteristics of steroid receptors in breast cancer were investigated to determine indicators of response to treatment for breast cancer. First, steroid receptors in breast cancer tissues were characterized by means of dissociation constants in tissues from premenopausal and postmenopausal patients; dissociation constants were determined with the aid of charcoal absorption at 4 C for estradiol-17beta-estrogen receptors (ERs), R5020-progesterone (PR) receptors, 5alpha-dihydrotestosterone (DHT)-androgen receptors (ARs), and R1881-ARs. These receptors sedimented to 7-6S and 5-4S regions; the 7-6S binding was easily dissociated with 5-20% sucrose gradient centrifugation. ARs and PRs were contained in the R1881-cytosol bindings. Cytosolic steroid receptor levels were analyzed in each case, and max binding sites were analyzed by Scatchard plot analysis. Nuclear receptors were determined by exchange assay; nuclear PRs and ARs were detected in a few cases, and nuclear ERs were detected while cytosolic ERs were not detected. Results of studies of nuclear binding of steroid receptor complexes substituting ERs and PRs of rabbit uterine cytosol for the human breast cancer tissues suggested that part or all of the nuclear receptor-binding sites of breast cancer tissues are defective in some tumor nuclei. The existence of receptors in the cytosol or nuclei, nuclear binding of receptor-steroid complexes, or measurement of nuclear RNA synthesis by steroid receptors in breast cancer cells were thought to be effective indicators of the endocrine-therapy response of breast cancer. (34 Refs) (In JPN)

38. HORMONE RECEPTORS IN MALE BREAST CARCINOMA.

Ruff SJ, Bauer JE, Keenan EJ, Moseley HS, Fletcher WS
(c/o Fletcher) Div. Surgical Oncology, Univ. Oregon Health Sciences Center, 3181 SW Sam Jackson Park Road, Portland, OR, 97201
J Surg Oncol; 18(1):55-59 1981

It is well established that approx 60% of female breast cancers contain estrogen receptors (ER+). The hormonal receptor status of male breast cancers remains relatively unknown. Tumor tissue from 14 patients has been reviewed at the University of Oregon Health Sciences Center. Specimens of all 14 patients were ER+ with a range of 5.5 to 374 fmol/mg protein. Eight of 12 patients had tumors which also contained progesterone receptors (PR+) with a range of 42 to 1,852 fmol/mg/protein. Nine patients were treated by modified radical mastectomy, two by radical mastectomy, one by simple mastectomy, and two by biopsies only. Twelve patients remain free of disease with a mean follow-up of less than 2 yr. The two patients who developed metastases both responded to endocrine ablation by orchiectomy and subsequent adrenalectomy. These data suggest that male breast cancer is highly endocrine sensitive and that endocrine ablation can play an integral part in those men unfortunate enough to develop disseminated disease. (Author abstract) (18 Refs)

39. A RANDOMIZED TRIAL COMPARING SURGICAL ADRENALECTOMY WITH AMINOGLUTETHIMIDE PLUS HYDROCORTISONE IN WOMEN WITH ADVANCED BREAST CANCER.

Santen RJ, Worgul TJ, Samojlik E, Interrante A, Boucher AE, Lipton A, Harvey HA, White DS, Smart E, Cox C, Wells SA
Div. Endocrinology, Milton S. Hershey Medical Center, Hershey, PA, 17033
N Engl J Med; 305(10):545-551 1981

A randomized clinical trial was used to establish whether surgical adrenalectomy is superior to a medical ablative approach to estrogen suppression using aminoglutethimide (AG) and hydrocortisone for the treatment of advanced breast cancer. Ninety-six postmenopausal or surgically oophorectomized women with inoperable, recurrent, or metastatic carcinoma of the breast were randomized to receive one of the two therapies. Before randomization, women were stratified according to disease-free interval, site of dominant disease, and estrogen-receptor status. Of 40 evaluable women treated with AG + hydrocortisone, 53% had objective responses, compared with 45% of 29 women undergoing surgery; the difference was not statistically significant. Objective tumor regression persisted for means of greater than 17.1 mo in the surgery patients and 17.2 mo in the medical group. No consistent differences were observed in the suppression of estrogens produced by the two therapies; in contrast, only AG + hydrocortisone preserved androgen production. Drug side effects include lethargy, dizziness, ataxia, skin rash, occasional hypothyroidism, and rare blood dyscrasias. While no women in the medical group had adrenal insufficiency, 5/29 in the surgical group had this problem at least once up to 2 yr after the operation. Given the demonstration that the surgical procedure is not superior to the medical, the medical approach could logically be chosen as a means to avoid major surgery and the required lengthy hospitalization in patients with metastatic breast carcinoma. (41 Refs)

40. THE TREATMENT OF METASTATIC BREAST CANCER WITH AMINOGLUTETHIMIDE.

Kaye SB, Woods RL, Fox RM, Tattersall MH
(c/o Tattersall) Dept. Medical Oncology, Ludwig Inst. Cancer Res., Univ. Sydney, Sydney NSW 2006, Australia
Aust NZ J Med; 11(4):370-374 1981

Thirty-eight patients with advanced breast cancer, resistant to prior endocrine therapy and in most cases prior chemotherapy, were treated with aminoglutethimide, 250 mg qds. Seven of 30 evaluable patients (23%) responded. Six have subsequently relapsed with a mean duration of response of 17 wk, while one continues to respond after 50 wk of therapy. Six additional patients (20%) had stable disease during aminoglutethimide therapy (mean duration of 16 wk). Three of the seven responders had shown a partial response, two had stable disease and two had progressive disease on prior endocrine therapy (including tamoxifen); six of the seven patients responding to aminoglutethimide had received prior combination chemotherapy, to which all had responded. Aminoglutethimide was generally well tolerated, although three patients withdrew from treatment within the first two wk because of intolerable drowsiness. Aminoglutethimide offers a useful alternative to surgical adrenalectomy for women with advanced breast cancer responsive to previous endocrine and cytotoxic chemotherapy. (Author abstract) (23 Refs)

41. CORTICOSTEROIDS FOR ELDERLY PATIENTS WITH BREAST CANCER.

Minton MJ, Knight RK, Rubens RD, Hayward JL
(c/o Rubens) Breast Unit, Guy's Hosp., London, SE1 9RT, England
Cancer; 48(4):883-887 1981

Ninety-one assessable elderly women (greater than or equal to 65 yr) with advanced breast cancer were treated with prednisolone 15 mg (or cortisone 75 mg) daily afte primary endocrine treatment (estrogens, androgens or tamoxifen). Thirteen (14%) achieved an objective regression, and 19 (21%) others showed no change for greater than or equal to 6 mo. Hence, 32 patients (35%) had control of disease for about 1 yr. Responses were mainly in soft tissue and skeletal lesions and were independent of response to prior endocrine treatment. Toxicity was low. Low-dose corticosteroid treatment is of value in controlling advanced breast cancer in elderly women. (Author abstract) (28 Refs)

42. LESS TOXIC TREATMENT FOR ADVANCED BREAST CANCER.

Henderson IC
Sidney Farber Cancer Inst., Boston, MA, 02115
N Engl J Med; 305(10):575-577 1981

Placed within the context of the variety of endocrine manipulations long used effectively to treat patients with metastatic breast cancer is the relatively new endocrine therapy, aminoglutethimide. The drug has been found to be safe, effective, and minimally toxic when compared with most other anticancer therapies. After its administration a fall in circulating estrogens similar to that seen after adrenalectomy is seen. This fall has been shown to result from inhibition of conversion of androstenedione to estrone in non-adrenal tissues. Tumor regression in some patients not responding to surgical adrenalectomy has also been observed after aminoglutethimide therapy. These results, together with relatively low toxicity and reversibility of action, make the drug a reasonable second therapy after tamoxifen in postmenopausal women and worthy of inclusion among effective treatments for breast cancer. (14 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

43. QUALITY OF LONG-TERM SURVIVAL FOLLOWING IRRADIATION FOR INTRACRANIAL TUMORS IN CHILDREN UNDER THE AGE OF TWO.

Spunberg JJ, Chang CH, Goldman M, Auricchio E, Bell JJ
Dept. Radiation Therapy, Albert Einstein Medical Center, York and Tabor Roads, Philadelphia, PA, 19141
Int J Radiat Oncol Biol Phys; 7(6):727-736 1981

Survival rates, quality of survival, and late radiation sequelae were studied retrospectively in 38 patients who received CNS irradiation alone or postoperatively for primary intracranial tumors at age 3-24 mo. The children included 21 females and 17 males. Twenty-four deaths were attributable to the primary disease or its complications. The 5-, 10-, and 15-yr absolute survival rates were 50%, 39%, and 38%, respectively. Posterior fossa tumors had the best prognosis. The 14 patients who are still alive have a mean survival of 12.9 yr (range 5-20 yr). Four of these patients had late recurrence of the primary tumor requiring additional radiotherapy and/or surgery. Of the long-term survivors, 8 have minimal or no neurologic deficits, 11 are within the educable range on formal intelligence tests, and 12 have a Karnofsky performance score of 70 or greater. Clinical evidence of endocrinologic dysfunction is limited to growth retardation in three children who received doses greater than 3,600 rad to the hypothalamic-pituitary region. On a 'Composite Quality of Survival Scale,' graded 1 to 5, eight patients rated grade 3 or better, with three patients essentially normal. The data indicated that children less than 2 yr tolerate cranial radiotherapy better than previously believed; however, further optimization of radiotherapy factors (dose, time, vol) is essential to minimize the potential late effects of CNS radiation. (63 Refs)

44. INAPPROPRIATE SECRETION OF THYROID-STIMULATING HORMONE.

Weintraub BD, Gershengorn MC, Kourides IA, Fein H
NIH, Building 10, Room 8N315, Bethesda, MD, 20205
Ann Intern Med; 95(3):339-351 1981

Recent studies have provided major new insights into the syndromes of inappropriate secretion of thyroid-stimulating hormone (TSH), a heterogeneous group of disorders in which patients show inappropriately elevated levels of serum immunoactive TSH in the presence of elevated free thyroid hormone levels. Certain of these patients appear to have a non-neoplastic disorder associated with variable degrees of pituitary and peripheral resistance to the action of thyroid hormone, whereas others harbor a tumor of pituitary thyrotropic cells. Measurement of free serum alpha subunit has proved valuable in differentiating these disorders, showing normal alpha concentration and alpha-to-TSH ratios in the non-neoplastic and highly elevated values in the neoplastic disorders. All these syndromes appear unrelated to Graves' disease because thyroid-bindi
and thyroid-stimulating antibodies are usually absent. Some
these patients also have abnormal metabolism of thyroid ho
mones. Although the pathogenesis of these syndromes remai
to be elucidated, increased recognition and study of these p
tients should provide fundamental insights into the regulatio
of TSH secretion as well as the action of thyroid hormon
(Author abstract) (85 Refs)

45. IV DICHLOROMETHYLENE DIPHOSPHONATE IN CANCER-ASSOCIATED HYPERCALCEMIA: A PHASE I-I EVALUATION.

Cohen AI, Koeller J, Davis TE, Citrin DL
(c/o Davis) Dept. Human Oncology, Univ. Wisconsin Clinical Canc Center, Madison, WI, 53792
Cancer Treat Rep; 65(7/8):651-653 1981

The first clinical evaluation of iv dichloromethylene dipho
phonate (Cl2MDP) in the treatment of hypercalcemia due t
malignant disease is described for 14 patients (9 males, 5 fe
males) with diagnoses of surgically unresectable or metastati
cancer. Cl2MDP was administered at a dose of 4-20 mg/k
body wt by 1-hr iv infusion. The patients were studied for 7
hr following infusion. During this time, the patient's clinica
condition and serum calcium levels were closely monitored
No major toxic effects were observed. Two patients treate
with 4 mg/kg Cl2MDP developed transient mild diarrhea fo
lowing infusion. Two patients had major gastrointestinal bleed
ing 5 and 30 days following treatment with Cl2MDP. Of th
15 patients, 10 responded to infusion of Cl2MDP with a de
crease in serum calcium of greater than 1 mg/100 ml. Six pa
tients had an early response, within 13 hr of infusion. In an
other four patients, the serum calcium decreased more slowly
Two nonresponding patients had an increase in serum calciu
over the study period. Overall the mean serum calcium level o
the group at the conclusion of the study was 11.6 +-4 mg/10
ml, compared with a prestudy mean of 13.1 +-3 mg/100 ml (
less than 0.001). The results indicated that iv Cl2MDP adminis-
tration can decrease serum calcium levels elevated due t
cancer. (9 Refs)

46. PREDICTION OF PROGRESSIVE DISEASE IN ZOLLINGER-ELLISON SYNDROME - COMPARISON OF AVAILABLE PREOPERATIVE TESTS.

Fabri PJ, Johnson JA, Ellison EC
Dept. Surgery, Ohio State Univ. Coll. Medicine, 410 West Tenth Ave., Columbus, OH, 43210
J Surg Res; 31(2):93-97 1981

Availability of alternative methods of treatment of the Zollinger-Ellison syndrome (ZES) has necessitated a reevaluation of that disease. To evaluate ability of preoperative tests to predict postoperative clinical course, serum samples (frozen since collection) obtained fasting and after calcium stimulation in 18 patients with documented ZES with at least 5 yr of postoperative follow-up were reassayed, fractionated into molecular components by gel filtration through a 200 x 1-cm Sephadex G-50 superfine column, and quantitated by assay with an antibody with equimolar recognition of the major C-terminal peptides. Total gastrin immunoreactivity (IRG), response of serum gastrin to calcium stimulation (SIRG), or the combination of these two factors are the most frequent criteria for estimating postoperative course and magnitude of disease. These measurements were compared to the percentage of G-17 (G-17/IRG) by the methods of R. S. Galen and S. R. Gambino (Beyond Normality; The Predictive Value and Efficiency of

Medical Diagnoses, New York: Wiley 1975) (Sensitivity, Specificity, Predictive value of positive and negative tests, Efficiency). Percentage G-17 greater than 20% of IRG is the most sensitive (100%) and specific (91%) method of evaluating exte nt of disease preoperatively in patients with ZES. (Author abstract) (13 Refs)

47. DIARRHEAL SYNDROME AND NON-BETA CELL TUMORS OF THE PANCREAS. VERNER MORRISON SYNDROME: ONE CASE REPORT.

Machado MC, Bettarello A, De Barros Mott C, Bacchella T, Monteiro da Cunha JE
Dep. de Clinica Cirurgica, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil
Rev Hosp Clin Fac Med Sao Paulo; 36(2):78-85 1981

A 56-yr-old woman was admitted with diarrhea of unknown origin, which appeared 2.5 yr ago with asymptomatic periods of up to a wk duration. Arteriography of celiac trunk indicated hepatic metastases. Computed tomography revealed hepatic metastases and a pancreatic corpus tumor which was invading the peripancreatic fat. At surgery a pancreatic tumor occupying the corpus and tail was resected. Metastases were observed in both liver lobes and in two retroperitoneal ganglions. Cholecystectomy was performed in view of future liver embolization, which was performed postoperatively. First the celiac hepatic artery and a few days later the superior mesenteric artery were embolized. After these procedures diarrhea stopped. Plasma separated from blood removed the night before the operation showed a high concentration of vasoactive intestinal polypeptide (VIP, 42 picomoles/g) and human pancreatic polypeptide (HPP, 1,000 picomoles/g) confirming the Verner Morrison syndrome. Concentrations of Ca and glucose in plasma were normal. Histalog gave normal gastric secretory response. Two mo postoperatively diarrhea reappeared, angiography revealed recanalization, especially of the superior mesenteric artery. New embolization was performed and chemotherapy (streptozotocin, adriamycin, and 5-fluorouracil) was started. After 12 mo the patient is completely asymptomatic. Cases presented in literature, problems concerning diagnosis and therapy are discussed extensively. (44 Refs) (In POR)

48. GUT HORMONES AND GUT ENDOCRINE TUMOR SYNDROMES.

Buchanan KD
Queen's Univ. Belfast, Royal Victoria Hosp., Belfast, Northern Ireland
J Appl Med; 7(7):533-537,539 1981

A brief discussion concerning the field of gut endocrinology is presented together with a description of the clinical and diagnostic features of the gut endocrine tumors (GETs). GETs most commonly arise in the pancreas or small bowel and have four main patterns: cord-like, ribbon, alveolar, and an undifferentiated trabecular or medullary structure. They are further histologically classified into those containing enterochromaffin cells and those containing nonenterochromaffin cells. An islet cell origin is common for tumors of the nonenterochromaffin cells. The enterochromaffin cell type of argentaffinomas arise commonly in the small bowel but may also occur in the bronchus, islets, stomach, biliary tract, and large bowel. Any pancreatic tumor or small-bowel tumor or an atypical bronchial tumor should be suspected of being a GET. GETs occurring in an unusual site, as well as hepatic metastases of GETs, may be confused with anaplastic carcinoma. GETs are not as invasive as nonendocrine cancers and have a relatively good prognosis. The most common clinical features are hepatic metastases, diarrhea, diabetes mellitus, and signs of a pancreatic mass. The clinical features and diagnostic methods for the following GETs are discussed in detail: carcinoid syndrome, insulinomas, Zollinger-Ellison syndrome, glucagonoma syndrome, Verner-Morrison syndrome, and somatostatinomas. Radiologic methods and hormone assays may be useful in the diagnosis of GETs. Selective celiac axis angiography is particularly useful for demonstrating insulinomas, and superior mesenteric and celiac axis angiography displays most carcinoid tumors. Other diagnostic methods include transhepatic sampling with hormone assays and multiple hormone assays in different possible venous drainage sites of the tumor. A table listing the clinical indications for specific hormone assays is provided. The author believes that an increased clinical awareness of the GET syndromes plus the development of screening programs may result in an earlier and increased number of diagnoses of GETs. (20 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

49. ECTOPIC ADRENOCORTICOTROPHIC (ACTH) SYNDROME AND SMALL CELL CARCINOMA OF THE LUNG--ASSESSMENT OF CLINICAL IMPLICATIONS IN PATIENTS ON COMBINATION CHEMOTHERAPY.

Abeloff MD, Trump DL, Baylin SB
Room 128, Oncology Center, Johns Hopkins Hosp., 600 N. Wolfe St., Baltimore, MD, 21205
Cancer; 48(5):1082-1087 1981

Small cell carcinoma of the lung is the tumor most commonly associated with ectopic ACTH production and hypercortisolism. The relationship between this paraneoplastic endocrine syndrome and the clinical course of the tumor is examined in this review of patients with the ectopic ACTH syndrome and small cell carcinoma seen at The Johns Hopkins Oncology Center between 1973 and 1979. Five of 157 (3.2%) patients with small cell carcinoma were clinically diagnosed as having the ectopic ACTH syndrome. The onset of this endocrine syndrome appeared to coincide with a more aggressive phase of the course of small cell carcinoma. Further analysis of these cases suggests that the development of the ectopic ACTH syndrome may reflect changes in cell populations within the tumor and/or alterations in tumor behavior with time and perhaps with the effects of drug therapy. (Author abstract) (20 Refs)

50. APUD CELLS IN TERATOMAS.

Bosman FT, Louwerens JW
Dept. Pathology, Univ. Medical Center, Wassenaarsweg 62, Leiden, The Netherlands
Am J Pathol; 104(2):174-180 1981

The origin of the endocrine cells in the respiratory tract and the gastrointesti nal tract is still a matter of debate. In the original concept of the amine precursor uptake and decarboxylation (APUD) system, all APUD cells were considered to be derived from the neural crest. More recently it has been proposed that the APUD cell types of the gastrointestinal and respiratory tracts originate from neuroendocrine-programmed ectoblast. Still other investigators have reported observations that favor a direct endodermal origin of these cell types. Based on the assumption that in teratomas different tissue types which in normal embryogenesis are derived from the neuroectoderm might be expected to occur together, we investigated a series of cystic ovarian teratomas and testicular teratocarcinomas for the presence of brain tissue and of different types of APUD cells. In the ovarian teratomas, intestinal and respiratory APUD cell types were found almost exclusively without coexistence of brain tissue, whereas melanocytes, which are of neuroectodermal origin, occurred mostly together with brain tissue. In the testicular teratocarcinomas, intestinal types of APUD cells occurred without brain tissue. Peptide hormone production was found in appropriate tissues. It can therefore be concluded that in teratomas appropriate intestinal and respiratory APUD cells differentiate in and presumably descend directly from intestinal and respiratory epithelium. (Author abstract) (32 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

51. SECRETION OF LH, FSH AND PRL SHOWN BY CELL CULTURE AND IMMUNOCYTOCHEMISTRY OF HUMAN FUNCTIONLESS PITUITARY ADENOMAS.

Mashiter K, Adams E, Van Noorden S

Endocrine Unit, Dept. Medicine, Royal Postgraduate Medical Sch., Hammersmith Hosp., Du Cane Road, London W12 OHS, England

Clin Endocrinol (Oxf); 15(2):103-112 1981

Hormone secretion by ten functionless human pituitary adenomas in cell culture has been measured, and compared with tissue immunocytochemistry and electron microscopy, as well as results with a normal pituitary. Patients presented following routine x-ray and had no clinical or biochemical endocrine abnormality apart from one male with raised serum FSH and PRL, normal LH, and low testosterone. Of the ten adenomas, nine secreted both LH and FSH in cell culture and five of these also secreted PRL, one did not secrete any anterior pituitary hormones (ACTH was not measured). No GH or TSH was detectable in the cultures of the nine LH/FSH secretors excluding the possibility of contamination by normal anterior pituitary. The normal pituitary cells secreted all anterior pituitary hormones; the amounts of FSH/LH being comparable with those of the adenomas. Immunostaining confirmed the cell culture results and showed the adenoma FSH/LH cells to be scattered singly or in small groups of two to five cells with both hormones usually being in the same cell. PRL where found was in separate cells. Hormone granules were small (50-160 nm), round or irregular and scattered in the cytoplasm of rounded cells of low secretory activity. The negatively staining cells were not different ultrastructurally to those staining positively. It is concluded that a significant proportion of functionless pituitary adenomas have detectable low levels of LH/FSH secretion often accompanied by PRL when examined by cell culture of immunocytochemistry. Although these adenomas were endocrinologically quiescent activity could have been masked because of postmenopausal secretion and one male probably had an FSH-secreting adenoma. (Author abstract) (32 Refs)

52. INCREASED LEVELS OF NEURON-SPECIFIC ENOLASE IN PC12 PHEOCHROMOCYTOMA CELLS AS A RESULT OF NERVE GROWTH FACTOR TREATMENT.

Vinores SA, Marangos PJ, Parma AM, Guroff G
Section on Intermediary Metabolism, Lab. Developmental Neurobiology, Natl. Inst. Child Health and Human Development, Bethesda, MD, 20205
J Neurochem; 37(3):597-600 1981

Treatment of PC12 pheochromocytoma cells with nerve growth factor (NGF) resulted in increased levels of neuron-specific enolase (NSE). Neither insulin, growth hormone, cytochrome c, nor sodium butyrate increased NSE levels. Epidermal growth factor (EGF) did increase NSE levels, although not to the same extent as NGF. As little as 1 ng/ml NGF induced the max increase in NSE. As PC12 cells increased in density, the NSE levels increased even in untreated cells. (Author abstract) (24 Refs)

53. EFFECTS OF LECTINS ON CAMP PRODUCTION AND STEROIDOGENESIS IN CULTURED ADRENAL TUMOR CELLS.

Lifrak E, Chen CC, Wishnow RM
Veterans Admin. Medical Center, Long Beach, CA, 90822
Exp Cell Res; 135(1):167-177 1981

The plant lectins, concanavalin A (conA), wheat germ agglutinin (WGA), and phytohemagglutinin (PHA) stimulate steroidogenesis in cultured adrenal tumor cells. ConA max stimulated steroidogenesis at 100 ug/ml following an approx 4 hr lag phase. ConA stimulation was completely inhibited by alpha-methyl-D-mannopyranoside and the WGA effect was prevented by N-acetyl-D-glucosamine. It was also found that conA alone did not cause a measurable increase in either intra- or extracellular cyclic AMP (cAMP) production. In addition, conA when added simultaneously with ACTH doubled the intra- and extracellular cAMP production over controls treated with ACTH alone. This enhancement effect was dose dependent. When Y-1 cells were preincubated with conA and then treated with either ACTH or cholera enterotoxin (CT) there was a dose- and time-dependent inhibition of induced cAMP production. In the case of CT, the inhibitory effect occurred even with simultaneous addition of conA and CT. This effect was reversed by addition of both alpha-methyl-D-mannopyranoside and washing with Eagle's minimal essential medium (MEM) 1 hr after CT had bound to its receptor. This reversal was not apparent for the inhibitory effect of conA on ACTH-induced cAMP production which occurred after 2 h of preincubation with conA. These results demonstrate that conA, as well as the other plant lectins, interact with specific membrane receptors to reversibly stimulate steroid production as well as enhancing or inhibiting ligand-induced cAMP production in cultured adrenal tumor cells. (Author abstract) (38 Refs)

54. INSULIN AND GLUCAGON IN RATS WITH ISLET CELL TUMORS INDUCED BY SMALL DOSES OF STREPTOZOTOCIN.

Yoshino G, Kazumi T, Morita S, Baba S
Room 7302, Medical Sciences Building, Univ. Toronto, Toronto, Ont., M5S 1A8, Canada
Can J Physiol Pharmacol; 59(8):818-823 1981

Plasma insulin and glucagon responses to oral glucose loading were examined in rats with islet cell tumors induced by a single iv injection of streptozotocin (30 or 40 mg/kg body wt). Twenty-four macroscopic and six microscopic tumors occurred in 21 rats. In 15 of 21 tumor-bearing rats, there was exaggerated insulin release in response to oral glucose. Plasma glucose levels did not rise with the oral glucose load and were comparable to those seen in normal animals. Hence these rats are described as having 'responsive tumors.' In six rats with 'nonresponsive tumors' there was no insulin response and the plasma glucose levels rose. No significant differences in plasma glucagon levels were observed between the two groups. Nonresponsive tumors as well as responsive tumors contained a significant amount of extractable insulin (17.68 +-8.60 and 35.07 +-10.05 mg/g wet wt, respectively) and detectable amounts of immunoreactive glucagon (1.47 +-0.61 and 2.24 +-0.67 ug/g wet wt, respectively). These results suggest that a small dose of streptozotocin produces two types of islet cell tumors. One is insulin producing and insulin secreting whereas the other is insulin producing but not insulin secreting. (Author abstract) (14 Refs)

55. ALLOTRANSPLANTATION OF INSULINOMA INTO THE TESTIS OF DIABETIC RATS.

Akimaru K, Stuhlmiller GM, Seigler HF
(c/o Seigler), Duke Univ. Medical Center, Box 3947, Durham, NC, 27710
Transplantation; 32(3):227-232 1981

We have previously shown that many of the metabolic abnormalities of the streptozotocin-induced diabetic state in KX (Ag-B7) rats can be corrected by a transplantable syngeneic insulin-secreting insulinoma. In this study, we have evaluated the transplantability of this KX insulinoma into allogeneic Sprague-Dawley (SD) rats (Ag-B6). Graft rejection was evident at 7 days post-transplant of the tumor when engraftment was made in a sc site. Prolonged graft survival was observed in 1 of 16 normal SD rats and in 3 of 19 streptozotocin-induced diabetic SD rats when the tumor was grafted into the testis. Mean survival times for these successful allografts was 27 +-4 days. Blood glucose levels in these animals returned to normal limits. Failure of the other intratesticular (IT) allografts was attributable to technical considerations rather than to specific antigraft immune reactions. Sensitization of SD rats with KX skin grafts or by sc injection of the KX insulinoma resulted in second-set survival times for subsequently applied KX skin grafts. Sera from animals sensitized in this manner contained antibody cytotoxic for KX lymphocytes, thus demonstrating the immunogenicity of the insulinoma. In contrast, SD rats sensitized by IT injection of the KX insulinoma rejected subsequent KX skin grafts with a primary antigraft immune reaction. Sera taken from SD rats which had unsuccessful IT engraftment of the insulinoma did not contain anti-KX antibody. These studies thus suggest that, although the KX insulinoma does express KX histocompatibility antigens, exposure of SD rats to these antigens via IT transplant fails to provoke an anti-KX immune response. Successfully engrafted insulinoma retains its metabolic activity as evidenced by its alleviation of the hyperglycemic state of the recipient diabetic animals. (Author abstract) (29 Refs)

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- SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS 35-42

PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. SINGLE PHOTON EMISSION TOMOGRAPHY OF THE PITUITARY: PRELIMINARY COMMUNICATION.

Britton K, Shapiro B
St. Bartholomew's Hosp., West Smithfield, London EC1A 7BE, England
J R Soc Med; 74(9):667-669 1981

A specific application of single photon emission tomography to the relative quantitation of the pituitary region is described together with the results obtained in 19 patients with pituitary adenoma proven by air encephalography. These are compared with those obtained by x-ray computer tomography and con-

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ventional brain imaging and a superiority of single photon emission tomography is demonstrated in this small series. (Author abstract) (4 Refs)

2. ANTERIOR PITUITARY HORMONE LEVELS IN THE CEREBROSPINAL FLUID OF PATIENTS WITH PITUITARY AND PARASELLAR TUMORS.

Braunstein GD, Hassen G, Kamdar V, Nelson JC
Cedars-Sinai Medical Center, Room 516, Schuman Building, 8700 Beverly Blvd., Los Angeles, CA, 90048
Fertil Steril; 36(2):164-172 1981

Cerebrospinal fluid (CSF) concentrations of growth hormone, prolactin (PRL), adrenocorticotropin, thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, and the glycoprotein hormone alpha subunit were determined in 30 patients with pituitary and parasellar tumors. Although many of the patients had elevated hormone levels, no differentiation between patients with intrasellar tumors and those with pituitary tumors with suprasellar extension or primary suprasellar tumors could be made based upon the absolute CSF hormone concentration. A highly significant correlation between serum and CSF PRL concentrations was found (r = 0.87; P less than 0.001), suggesting that CSF PRL is derived from the serum. No correlation was found between the serum and CSF concentrations of the other anterior pituitary hormones. (Author abstract) (25 Refs)

3. PAPILLEDEMA IN TWO PATIENTS WITH ACROMEGALY AND INTRASELLAR PITUITARY TUMORS.

Mueller GL, McKenna TJ, Kelly G, O'Day DM, Hollifield JW, Pidgeon C, Hutchinson M, Rabin D
Endocrinology Service, Wilford Hall Medical Center, Lackland AFB, TX, 78236
Arch Intern Med; 141(11):1491-1495 1981

Two patients had bilateral papilledema complicating acromegaly. Both patients had enlarged blind spots, but otherwise visual fields were normal. Suprasellar extension of the pituitary tumors was diligently sought with the use of visual field examination, pneumoencephalography, internal carotid arteriography, and computed axial tomography, and tumor extension did not exist. Transsphenoidal and transethmoidal routes were used to perform partial hypophysectomies in these patients. The procedure was completely successful in one patient and partially successful in the other patient. After hypophysectomy, papilledema resolved in both patients. This beneficial effect may be the result of anatomical changes, the reduction in growth hormone levels, or both. These observations suggest that the pathogenesis of papilledema that occurs in association with acromegaly may be different from papilledema that occurs secondary to suprasellar expansion of pituitary tumors. (Author abstract) (11 Refs)

4. CRANIOPHARYNGIOMA IN TWO SIBLINGS.

Vargas JR, Pino JA, Murad TM
4949 Mountain View Parkway, Birmingham, AL, 35244
JAMA; 246(16):1807-1808 1981

The cases of two siblings (a 16-yr-old boy and his sister who was 2-yr younger) who each had gradual symptomatic development of diabetes insipidus and panhypopituitarism and were later found to have craniopharyngiomas are reported. The boy, prepubertal at the time of examination (age 16), had bitemporal hemianopsia, bilateral nasal optic disc atrophy, and a generalized enlargement of the sella turcica. The pituitary was removed during transfrontal exploratory surgery and was reported as craniopharyngioma. The patient's postoperative course was uneventful; he received cortisone, levothyroxine, sodium, and vasopression tannate in oil. The patient grew 7 cm during the next 19 mo, but he did not show sexual maturation. The girl was first treated at age 16 for neurogenic diabetes insipidus. One yr later, the patient was examined for headaches of 6-mo duration and amenorrhea of 1-yr duration; some cardiac abnormalities were noted, and a test with levodopa did not increase growth hormone concentrations. Seventeen mo later, abnormal polytomograms were obtained, and the patient underwent transsphenoidal removal of a craniopharyngioma. Postoperative recovery was uneventful, and the patient was given hormone replacement therapy. No genetic studies were performed; it was thought that the occurrence of craniopharyngiomas in the siblings may have been coincidental. (10 Refs)

5. SUBDURAL EFFUSION FOLLOWING RADICAL SURGERY FOR CHIASMAL REGION TUMORS IN CHILDREN. REPORT OF 4 CASES.

Mizoi K, Takaku A, Suzuki J
Div. Neurosurgery, Inst. Brain Diseases, Tohoku Univ. Sch. Medicine, 5-13-1 Nagamachi, Sendai 982, Japan
Childs Brain; 8(4):307-315 1981

Cases of four children with subdural effusion occurring after radical surgery for chiasmal region tumors are reported. The patients were a 14-yr-old boy, a 6-yr-old girl, a 4-yr-old girl, and a 10-mo-old girl. The first three had craniopharyngiomas, the last, an optic glioma. At admission, all were alert but the third child. All had visual disturbances and developmental disturbances, one had a choked disc, three optic atrophy, and one hydrocephalus. The tumors were totally removed by bifrontal craniotomies. Symptoms of the subdural effusion were headache and nausea, visual disturbance, consciousness disturbance, and convulsions, in the four patients, respectively. All but the second patient underwent subduroperitoneal shunting. At follow-up, the first three patients had excellent results, the fourth died after discharge. In two patients, the pathogenetic mechanisms of this disorder are explained by a change from internal to external hydrocephalus or brain atrophy. The subdural effusion was either of 'serious type' which presented with severe symptoms or 'mild type' which was virtually asymptomatic. (10 Refs)

6. GERMINOMA OF THE PINEAL BODY AND THE WALL OF THIRD VENTRICLE - A REPORT OF FOUR CASES AND REVIEW OF LITERATURE..

Chen Z
Dept. Pathology, Xinjiang Medical Coll., Xinjiang Province, Reoples Republic of China
Zhonghua Zhongliu Zazhi; 3(1):22-25 1981

Primary tumors of the pineal body are relatively rare and their nomenclature and classification are confusing. Clinicopathological findings are described for four cases (2 males, 2 females, aged 8-15 yr) of germinoma of the pineal body and the wall of the third ventricle, which had originally been diagnosed erroneously as pinealoma or ectopic pinealoma. The major clinical characteristics included diabetes insipidus (in the 2 girls), macrogenitosomia praecex (in the 8-yr-old boy), increased intracranial pressure and other central nervous disorders. The literature is reviewed and the classification, nomenclature, histological structure, etiology and important clinical symptoms of primary tumors of the pineal body and third ventricle are discussed. (20 Refs) (In CHI)

THYROID TUMORS

7. MEASUREMENT OF VOLUME OF GOITER BY COMPUTED TOMOGRAPHY.

Toda M, Ohta F, Koike Y, Hosoi H
Dept. Otolaryngology, Kinki Univ. Sch. Medicine, Osaka 589, Japan
Nippon Jibiinkoka Gakkai Kaiho; 84(1):18-23 1981

Computed tomography (CT) was used to estimate the vol of goiters in one patient with a thyroid cyst, one with adenomatous goiter, two with thyroid cancer. The estimates calculated from CT findings were compared to the vol of the goiters which was determined by surgical and clinical findings. The goiters were imaged without enhancement with a General Electric CT/TX2 CT apparatus. The CT slices were processed by a Laitz ASM-type semiautomatic pattern analysis apparatus, and the vol of the goiter was determined from the patterns with a Hewlitt-Packard System 45-type small computer. The estimated goiter vol as determined with CT and the goiter vol of unilaterally resected surgical specimens from the patient with the thyroid cyst, the patient with the adenomatous goiter, and the two patients with thyroid cancer differed by 5%, 9.5%, 4.3%, and 0%, respectively. On the basis of studies of pre- and postoperative vol of goiters in three cases of Grave's disease, max error for calculating postsurgical remnant thyroid vol with CT was 1 g. This method of determining goiter vol with CT was thought to have clinical applications. (9 Refs) (In JPN)

8. IMPROVED QUALITY OF THYROID SCINTIGRAMS BY USING A GAMMA CAMERA AND PIN-HOLE COLLIMATOR.

Anger K, Feine U, Kaiser E
Nuklearmedizinische Abteilung des Medizinischen Strahleninstituts, Universitat Tubingen, Rontgenweg 11, D-7400 Tubingen, W. Germany
ROEFO; 135(2):188-192 1981

Thyroid scintigraphy with rectilinear scanner and with scintillation camera with pin-hole collimator (SCPC) was compared in 25 patients examined with 99mTc for diagnostic purposes (Group 1) and in 42 patients 3-5 days after radioiodine treatment. The findings obtained by the two methods were identical in 8/25 cases in Group 1 and in 19/42 cases in Group 2, but SCPC yielded additional clinical information in 8/25 and 10/42 cases, respectively. The SCPC method has a higher resolution than the scanner method. Diffuse goiter often showed additional cold nodules or areas with increased radioactivity, ie, microadenomas. Central cold areas were visualized by SCPC in some cases which were solitary adenomas in the rectilinear scan. (8 Refs) (In GER)

9. THE SIGNIFICANCE OF I-131 SCAN DOSE IN PATIENTS WITH THYROID CANCER: DETERMINATION OF ABLATION: CONCISE COMMUNICATION.

Waxman A, Ramanna L, Chapman N, Chapman D, Brachman M, Tanasescu D, Berman D, Catz B, Braunstein G
Dept. Nuclear Medicine, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, CA, 90048
J Nucl Med; 22(10):861-865 1981

Twenty-four patients with differentiated thyroid cancer were studied with diagnostic I-131 neck and chest scans after having undergone bilateral subtotal thyroidectomy and initial I-131 therapy with either 30-or 100-mCi doses. With an endogenous stimulation protocol, follow-up studies were performed with neck and chest scans using 2 and 10 mCi I-131. A 400% increase in sensitivity was found with a 10-mCi dose relative to a 2-mCi dose. Comparison with therapeutic doses of 30 and 100 mCi resulted in further increases in the detection of residual iodine-avid tissue. We conclude that a 2-mCi or lower dose of I-131 is inadequate in evaluating residual iodine-avid tissue visually in patients with thyroid cancer. The study does not answer the critical question of whether it is necessary to treat a patient presenting a negative 2-mCi but a positive 10-mCi scan. It may be appropriate to define ablation visually as well as clinically, with further studies directed toward determining a treatment rationale in this patient population. (Author abstract) (16 Refs)

10. REEVALUATION OF NEEDLE ASPIRATION CYTOLOGY IN DETECTION OF THYROID CANCER.

Rosen IB, Wallace C, Strawbridge HG, Walfish PG
Univ. Toronto, 600 University Ave., Suite 445, Toronot, Ontario, M5G 1X5, Canada
Surgery; 90(4):747-756 1981

From July, 1978, to August, 1980, 379 patients with thyroid disease were assessed clinically and underwent scintiscanning and needle aspiration cytology. One hundred fifty-three patients were selected for operation; there were 138 solid lesions and 15 cystic lesions. Selection criteria included clinical factors as well as cytology results. There was a cancer rate of 33% and a neoplasia rate of 92%. In the solid lesions there was a 36% incidence of cancer, whereas the incidence was 27% in cystic lesions. There was a false positive rate of 1%. A false negative rate could be viewed in various ways. Twenty-four cancers were missed in benign cytology for an incidence of 25%; however if one excluded the cytologic abnormal group, as some authors do, labeling them as potential malignancies, false negative results occurred in the cytologic benign cases for a rate of 4% for the entire group. If noncystic benign lesions alone were considered, the false negative rate would be 1%. False negative reporting arises predominantly from the inability to differentiate follicular adenoma from adenocarcinoma in cytology. Other factors such as geographic miss cystic disease also play a role. If one is to avoid underdiagnosis and undertreatment of thyroid cancer, one should consider cellular aspirates as potentially malignant and subject to surgical excision. Needle aspiration cytology has an unassailable role in the management of the patient with thyroid disease but requires interpretation in the light of clinical and scintiscanning results. (Author abstract) (10 Refs)

11. A FLOW CYTOMETRIC DEOXYRIBONUCLEIC ACID ANALYSIS OF PAPILLARY THYROID CARCINOMA.

Johannessen JV, Sobrinho-Simoes M, Tangen KO, Lindmo T
Dept. Pathology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Lab Invest; 45(4):336-341 1981

We present the first comprehensive flow cytometric analysis of papillary carcinoma of the human thyroid. All but 1 of the 22 papillary carcinomas showed a unimodal distribution of the nuclear DNA content. The mean modal DNA was significantly lower in papillary carcinomas than in normal thyroid tissue, a finding which is contradictory to some earlier reports based on conventional cytophotometry. Tumors predominantly composed of Hurthle cells had a significantly higher mean modal DNA, whereas no significant difference was found between tumors with many ground glass nuclei and those lacking this nuclear feature. A very low percentage of S-phase cells was found both in the primary tumors and their metastases. This percentage was even lower than in normal thyroid tissue. The low proliferative activity may in part explain why most papillary thyroid carcinomas run such a surprisingly indolent course even after the establishment of regional lymph node metastases. (Author abstract) (34 Refs)

12. LOCALLY INVASIVE, WELL-DIFFERENTIATED THYROID CANCER. 22 YEARS' EXPERIENCE AT MEMORIAL SLOAN-KETTERING CANCER CENTER.

Cody HS, Shah JP
Memorial Hosp., (c/o Shah) 425 East 67th St., New York, NY, 10021
Am J Surg; 142(4):480-483 1981

Our experience with 32 cases of locally invasive well-differentiated thyroid carcinoma suggests the following: (1) Thyroidectomy may be limited to the area of gross tumor involvement with little risk of recurrence in the normal opposite lobe. (2) Elective neck dissection should be considered in patients with locally invasive tumors since the incidence of nodal metastases is high. As observed in this study, occult metastases were present in five of six patients dissected electively, and nodal metastases developed later in four of eight patients observed. (3) Surgical procedures for the primary tumor should remove all gross disease. This is possible with conservative operations in most patients; the only deaths from uncontrolled local disease occurred in two patients in whom gross disease was left at the first procedure. Most deaths were caused by distant metastases, and the 5, 10 and 15 yr survival rates were 86, 64 and 64%, respectively. (Author abstract) (11 Refs)

13. EARLY THYROID CARCINOMA.

Gol'bert ZV, Demidov VP, Voronetskii IB
P. A. Hertsen Oncological Inst., Moscow, USSR
Sov Med; (7):40-45 1981

To enhance the detection of early forms of thyroid cancer in high risk groups, 496 patients with nodular thyroid lesions were subjected to histological examination. The patients were divided into two groups. Group I included 323 patients (29 men, 294 women; 9-73 yr old) undergoing primary surgery for nodular thyroid lesion, and Group II included 173 patients (37 men, 136 women; 13-74 yr old) undergoing repeated surgery after primary nonradical treatment (166 underwent enucleation or intracapsular resection). In Group I, early cancer of the thyroid was detected in 93/323 patients (69/224 had adenoma, 19/79 had chronic nonspecific thyroiditis, and 5/20 had nodular goiter). Multiple foci of III degree of dysplasia were observed in 66/93 patients. Of 93 early tumors, 41 had histology of follicular carcinoma, 22 of follicular-solid carcinoma, 22 of papillary carcinoma, and 8 originated from Ashkenasi cells or C-cells. Treatment of choice for the patients with early carcinomas was extrafascial hemi- and subtotal resection of the thyroid. Analysis of Group II showed residual tumor in 48.6% of the patients, anaplastic carcinoma in 9.5%, and metastases to the regional lymph nodes in 42.8%. (11 Refs) (In RUS)

14. HETEROGENEITY OF IMMUNOREACTIVE CALCITONIN IN EXTRACTS OF NORMAL HUMAN THYROID.

Woloszczuk W, Kovarik J
Ludwig Boltzmann-Institut fur Klinische Endokrinologie, Garnisong. 13, A-1090 Vienna, Austria
Horm Metab Res; 13(8):460-463 1981

Immunoreactive calcitonin in serum of patients with medullary carcinoma of the thyroid and in extracts of this tumor has been found to exhibit heterogeneity when analyzed by gel-chromatography and radioimmunoassay. In this study normal human thyroid tissue was homogenized in buffered saline at neutral pH and a soluble fraction was obtained after ultracentrifugation. Extracts were analyzed by gel-filtration before and after treatment with detergents, with denaturing agents and after reduction and alkylation. The stability in vitro of the extracted immunoreactive calcitonin was determined at different temperatures and the changes in heterogeneity analyzed by gel-filtration. The results suggest that at least part of the largest form of immunoreactive calcitonin is an artefact of the chromatographic procedure. Moiet ies with a mol wt below 12,000 Daltons were present and could be identical with prehormones described by others. However, no indication for a sequential degradation releasing calcitonin monomer from larger precursors was found in normal thyroid. (Author abstract) (14 Refs)

15. CHILDHOOD THYROMEGALY: RECENT DEVELOPMENTS.

Reiter EO, Root AW, Rettig K, Vargas A
(c/o Root) Dept. Pediatrics, All Children's Hosp., 801 6th St. South, St. Petersburg, FL, 33701
J Pediatr; 99(4):507-518 1981

Newer aspects of the causes, diagnosis, and management of goiter in the child and adolescent are reviewed. Thyroid immunology is discussed. Etiology and pathogenesis, clinical manifestations, laboratory evaluation, and treatment and prognosis of Hashimoto thyroiditis and Graves disease are presented. Other types of thyromegaly are described. In children, 17-40% of solitary nodules are malignant. A significant association exists between thyroid neoplasms and ionizing radiation to the head and neck. In one study of 2,189 young adults who had irradiation to the tonsils and nasopharynx between 1 and 12 yr of age, nodular disease of the thyroid was present in 713. Thyroid carcinoma was found in 11.2% of these patients. Differential diagnosis of thyroid neoplasms is discussed. Neoplastic lesions are usually discrete. Enlarged metastatic cervical lymph nodes are present in 67-85% of children with thyroid cancer; approx 14% of patients have pulmonary metastases at the time of diagnosis. Thyroid function is usually normal in children with thyroid carcinoma. The presence of a hard, fixed, solid mass (especially in the male), signs of metastasis or invasion (hoarseness, cervical adenopathy), rapid growth of the mass, and a history of irradiation are indications for open surgical biopsy. The combined use of ultrasonography and fine needle aspiration has greatly enhanced diagnostic accuracy and has permitted greater operative selectivity, especially in adults. Surgery, radioiodine ablation, and suppressive doses of thyroid have been employed in the treatment of differentiated thyroid carcinoma. (81 Refs)

PARATHYROID TUMORS

16. PARATHYROID AUTOTRANSPLANTATION IN PATIENTS WITH PARATHYROID DISEASE AND TOTAL THYROIDECTOMY. INDICATIONS IN 117 CASES.

Katz AD
Cedars-Sinai Medical Center, 8635 West 3rd St., Suite 695-W, Los Angeles, CA, 90048
Am J Surg; 142(4):490-493 1981

Parathyroid autotransplantation is a known and increasingly utilized procedure. It is indicated in patients with primary parathyroid hyperplasia, in patients with primary hypercalcemia who have normal parathyroid tissue devascularized during surgery, in patients with secondary and tertiary parathyroid hyperplasia, and in patients with total thyroidectomy when normal parathyroid tissue is accidentally or unavoidably removed or completely devascularized. No normal viable parathyroid tissue should be autotransplanted. This procedure was performed in 13 dialysis patients, 27 primary hypercalcemic patients and 77 patients with thyroidectomy. The hypercalcemic patients had autotransplantations into muscle pockets in the volar surface of the forearm, while the thyroidectomy patients had autotransplantation into the sternocleidomastoid muscles. The application of parathyroid autotransplantation is a major technical and physiologic breakthrough in the field of thyroid and parathyroid surgery. It should greatly reduce the morbidity associated with permanent hypocalcemia in this type of extensive surgery. (Author abstract) (23 Refs)

ADRENAL TUMORS

17. COMPUTER TOMOGRAPHY IN ADRENAL DIAGNOSTICS.

Luning M, Petzschmann E, Potzschke B
Institut fur Rontgendiagnostik (Charite), Schumannstrasse 20/21, DDR-1040 Berlin, E. Germany
Dtsch Gesundheitswes; 36(35):1445-1451 1981

Computer tomography is a non-invasive method for the confirmation and the exclusion as well as for determining the stage and extension of adrenal tumors suspected on the basis of clinical and paraclinical findings. After describing the normal picture and computer-tomographic criteria of pathological adrenals, the authors report their own results of CT-investigations in 47 patients with the tentative diagnosis of adrenal disorder (CT-findings: 31 times unconspicuous, 16 times pathological). Exact data on the degree of accuracy cannot yet be given. Nevertheless, some influences of computer-tomography on the entire diagnostic program may already be named. In the first place this will be a reduced or more purposeful use of angiographic and scintigraphic procedures. (Author abstract) (23 Refs) (In GER)

18. PERCUTANEOUS BIOPSY OF ADRENAL TUMORS.

Zornoza J, Ordonez N, Bernardino ME, Cohen MA
Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. Tumor Inst., Houston, TX
Urology; 18(4):412-416 1981

Percutaneous needle biopsy of adrenal masses was performed in 21 patients. Adrenal cysts, metastases, primary tumors, and a myelolipoma were diagnosed with a success rate of 81%. No complications were encountered. We concluded that percutaneous biopsy of adrenal masses is very useful in the management of selected patients. (Author abstract) (21 Refs)

19. VESICAL PHEOCHROMOCYTOMA.

Del Rio Prego A, Paredero del Bosque V, Martin Paredero V, Vela-Navarrete R, Rapado A, Castrillo JM
Clinica Nuestra Senora de la Concepcion, Fundacion Jimenez Diaz, Madrid, Spain
Rev Clin Esp; 161(5/6):347-350 1981

The 41 pheochromocytomas treated were situated in the right suprarenal region (20), in the left suprarenal area (16), bilaterally (2), in the Zuckerkandl organ (2), or in bladder paraganglia (1). The last case (40-yr-old male, blood pressure 300/150) is presented in detail. Urography showed deformed, compressed bladder due to large tumor. Aortography indicated normal aorta, suprarenal arteries, and glands, and richly vascularized bladder tumor. An orange-sized tumor was removed; blood pressure returned to normal as in the other cases. Embryological evolution of the chromaffin system is presented to explain the possible extra-suprarenal locations of this type of tumor. (22 Refs) (In SPA)

20. CATECHOLAMINE EXCRETION IN TUMORS OF CHROMAFFIN ORIGIN.

Traba ML
Unidad Metabolica, Fundacion Jimenez Diaz, Madrid, Spain
Rev Clin Esp; 162(1/2):15-19 1981

Forty cases were studied: 34 pheochromocytoma diagnosed clinically and confirmed surgically, and 6 neuroblastoma, 4 of which had surgery and radiotherapy. Catecholamines determined in urine were adrenalin, noradrenalin, metanephrine, vanillylmandelic acid (VMA), and homovanillic acid (HVA). Catecholamine quotients were calculated. The two tumors could be differentiated on a biochemical level: an increase in the VMA pathway in pheochromocytoma and in the HVA pathway in neuroblastoma was found. The VMA/HVA quotient was also useful for differentiation of tumor malignancy and intra- or extra-adrenal location. Neuroblastoma treatment could be normalized using the VMA/HVA quotient. In pheochromocytoma no correlation was observed between size of tumor and the amount of catecholamines excreted. (17 Refs) (In SPA)

21. HLA TRACERS AND CUSHING'S SYNDROME.

Luton JP, Baulieu F, Fumeron F, Hors J, Bricaire H
Centre de Recherches endocrinologiques, Hopital Cochin, 27, rue du Faubourg Saint-Jacques, F 75674 Paris Cedex 14, France
Ann Endocrinol (Paris); 42(1):3-9 1981

The frequency of human leukocyte antigens (HLA), 11 at locus A, and 17 at locus B, was determined in 38 patients with Cushing's syndrome. Of the 38 patients, 29 had Cushing's disease (4 with pituitary tumors), 8 had adrenal tumors (4 malignant adrenocortical tumors, 3 adenomas, and 1 Meador syndrome), and 1 had paraneoplastic hypercorticism with no identifiable primary tumor. The symptomatology (obesity, osteoporosis, amyotrophy, virilization, menstrual irregularities, and diabetes) of these patients is described. HLA antigens were also studied in 591 controls. No significant increase in HLA-A or B was observed among the patients. Meanwhile, the frequencies of antigens A11 and A29 were found in to be increased (24% in 2 patients) in Cushing's syndrome patients as compared with controls (12% and 11% for A11 and A29, respectively). The frequency of HLA-B8 was also increased in Cushing syndrome patients (28%) as compared with controls (17%). The significance of these findings is discussed. (12 Refs) (In FRE)

PANCREAS TUMORS

22. OPERATIVE AND CHEMOTHERAPEUTIC MANAGEMENT OF MALIGNANT GLUCAGON-PRODUCING TUMORS .

Prinz RA, Badrinath K, Banerji M, Sparagana M, Dorsch TR, Lawrence AM

Dept. Surgery, Loyola Univ. Medical Center, 2160 South First Ave., Maywood, IL, 60153

Surgery; 90(4):713-719 1981

Glucagon-producing tumors of the pancreas are among the rarest forms of islet cell tumors. Two patients are described in whom the characteristic dermatitis, glucose intolerance, wt loss, and anemia of the glucagonoma syndrome were due to a metastasizing islet cell carcinoma. In both, removal of the primary tumor with a distal pancreatectomy brought marked relief of all clinical symptoms for 1-and 2-yr periods. Because streptozocin, the usual chemotherapeutic agent for these tumors, is quite toxic and frequently unsuccessful, dimethyltriazenoimidazole carboximide (DTIC) was used for recurrence after operation. The first patient began taking DTIC when his rash reappeared and his immunoreactive glucagon (IRG) level rose to 6,000 pg/ml (normal, less than 200 pg/ml). Within 3 mo, his rash was gone, and IRG level was 75 pg/ml. The second patient developed a neoplastic gastrocolic fistula and was extremely emaciated. With DTIC, the fistula healed, and he gained wt and returned to work. His IRG level has decreased from 2,975 to 200 pg/ml. No side effects were noted during chemotherapy. Temporary palliation of malignant glucagon-producing neoplasms can be achieved by cytoreductive surgery. When the life-threatening symptoms of this syndrome recur, DTIC chemotherapy seems indicated because of its safety and effectiveness. (Author abstract) (13 Refs)

23. UPDATE ON PANCREATIC POLYPEPTIDE AS A SPECIFIC MARKER FOR ENDOCRINE TUMOURS OF THE PANCREAS AND GUT.

Oberg K, Grimelius L, Lundqvist G, Lorelius L-E

Dept. Internal Medicine, Univ. Hosp., S-750 14 Uppsala, Sweden

Acta Med Scand; 210(3):145-152 1981

Serum levels of pancreatic polypeptide (PP) were determined in 31 patients with endocrine tumors, localized in the pancreas (n = 16), small intestine (n = 13) and respiratory tract (n = 2). Two further patients with laxative abuse were investigated. Elevated serum levels in the peripheral circulation were noted in 56% of the patients with pancreatic tumors, in 60% of those with gut or bronchial tumors and in both patients with laxative abuse. Our study suggests that the elevated PP concentrations found in connection with endocrine gastrointestinal tumors originate from non-tumor pancreatic PP cells and only occasionally from the tumor. PP is a valuable tumor marker for endocrine gastrointestinal tumors, although it is not specific for pancreatic tumors. Certain inflammatory diseases, renal function and consumption of laxatives must be considered when evaluating elevated PP levels. Serum PP seems to be of limited value for evaluating the response to cytotoxic therapy. (Author abstract) (19 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

24. EXPERIMENTAL AND CLINICAL ASPECTS OF HORMONE THERAPY OF BREAST CANCER.

Maass H, Jonat W

Frauenklinik, Zentralkrankenhaus St. Jurgenstrasse, D-2800 Bremen, W. Germany

Arch Geschwulstforsch; 51(7):623-629 1981

Recent studies on the hormone therapy of advanced breast cancer are reviewed. Patients with relatively slowly growing tumors especially in the premenopausal period, patients with soft-tissue and lung metastases, and patients beyond the first 5 yr of menopause respond favorably to endocrine therapy. However, the remission rate in unselected patients is only 20-40% after ovariectomy, adrenalectomy, hypophysectomy, or androgen, estrogen, antiestrogen, or gestagen treatment. The determination of steroid hormone receptors is at present the best method for selecting the patients for endocrine therapy. The analysis of 1,336 cases showed a remission rate of 56% for estrogen receptor (ER)-positive and only 5.6% for ER-negative patients. A cooperative study covering 358 cases revealed remission rates of 77% for ER-positive and progesterone receptor (PR)-positive patients, 27% for ER-positive but PR-negative patients, 46% for ER-negative but PR-positive patients, and 11% for ER- and PR-negative patients. (16 Refs) (In GER)

25. SIGNIFICANCE OF SERUM CONCENTRATIONS OF CARCINOEMBRYONIC ANTIGEN, FERRITIN, AND CALCITONIN IN BREAST CANCER.

Bezwoda W, Derman D, Bothwell T, MacPhil P, Levin J, De Moor N
Dept. Medicine, Medical Sch., Hospital St., Johannesburg, S. Africa
Cancer; 48(7):1623-1628 1981

Serum concentrations of carcinoembryonic antigen (CEA), ferritin, and calcitonin were measured in 107 patients with breast cancer, 80 of whom had overt or occult metastatic disease. CEA and ferritin values were statistically higher in those patients with metastases. In contrast, there was no correlation between calcitonin concentrations and the stage of the disease. All 27 subjects with CEA concentrations greater than 80 ug/liter and 32 of 40 with values between 41-80 ug/liter had metastatic disease. Ferritin was a definite but less sensitive discriminator, with metastatic disease present in all nine patients having concentrations greater than 400 ug/liter. Such metastases were invariably hepatic. When the two measurements were used as a combined discriminant, the diagnostic accuracy increased somewhat. All 32 patients with a CEA concentration greater than ug/liter and/or a ferritin concentration greater than 400 ug/liter had metastatic disease; the same was true for 32 of the 42 subjects with CEA concentration between 41-80 ug/liter and/or a ferritin concentration between 200-400 ug/liter. The measurements and prognostic value, both when assessed alone and together, with a median survival from the time of study are significantly shorter in those with the highest values. (Author abstract) (23 Refs)

26. THE RESPONSE OF METASTATIC ADENOCARCINOMA OF THE PROSTATE TO EXOGENOUS TESTOSTERONE.

Fowler JE, Whitmore WF

(c/o Whitmore) Urologic Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

J Urol; 126(3):372-375 1981

In a retrospective review the response of 67 patients with metastatic adenocarcinoma of the prostate to the administration of exogenous testosterone was analyzed. Among 52 patients in whom objective and/or subjective responses were evaluable 45 experienced unfavorable responses. There was prompt regression of most unfavorable responses with testosterone withdrawal. The duration of treatment required to evoke an unfavorable response was related to the clinical status of the patient. Twenty-five percent of patients with symptomatic metastases who had received no prior treatment, 36% in symptomatic remission after endocrine therapy and 94% with symptomatic relapse after endocrine therapy experienced unfavorable responses within 30 days of treatment. No patient had objective evidence of tumor regression during testosterone therapy but seven patients, six with remission and one untreated, experienced symptomatic benefit. We conclude that the response of patients with metastatic prostate cancer to exogenous testosterone is related to the mass and endocrine treatment status, and that exogenous testosterone can stimulate prostatic neoplasms that proliferate in the absence of normal endogenous testosterone levels. (Author abstract) (14 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

27. LONG-TERM FOLLOW-UP OF OVARIAN FUNCTION IN WOMEN TREATED WITH MOPP CHEMOTHERAPY FOR HODGKIN'S DISEASE.

Schilsky RL, Sherins RJ, Hubbard SM, Wesley MN, Young RC, DeVita VT

Building 10, Room 12N226, Bethesda, MD, 20205

Am J Med; 71(4):552-556 1981

Twenty-seven women previously treated with MOPP (mechlorethamine, vincristine, procarbazine, prednisone) chemotherapy were evaluated to determine the status of ovarian function. All patients had completed therapy a median of 9 yr earlier and had a median age of 30 yr at the time of evaluation. Persistent amenorrhea has occurred in 11 of 24 patients (46%) treated with MOPP alone or MOPP plus radiation excluding the pelvis. Of patients with amenorrhea, 89% were older than age 25 at the time of treatment. In contrast, 80% of patients younger than age 25 at treatment continue to menstruate regularly. The time from diagnosis to amenorrhea was significantly shorter in the older patients ($p = 0.001$). Evaluation of serum gonadotropin and estradiol levels confirms ovarian failure as the cause of amenorrhea in all patients. Overall, these 27 patients have borne 13 normal children subsequent to chemotherapy. This long-term follow-up study demonstrates that chemotherapy-induced ovarian failure is age-related, that ovarian failure is often gradual in onset following the completion of chemotherapy and that, to date, the children born of women treated with this chemotherapy regimen appear to be entirely normal. (Author abstract) (17 Refs)

28. EFFECTS OF HIGH-DOSE METHOTREXATE AND VINCRISTINE ON OVARIAN AND TESTICULAR FUNCTIONS IN PATIENTS UNDERGOING POSTOPERATIVE ADJUVANT TREATMENT OF OSTEOSARCOMA.

Shamberger RC, Rosenberg SA, Seipp CA, Sherins RJ

(c/o Sherins) Developmental Endocrinology Branch, Natl. Inst. Child Health and Human Development, NIH, Bldg. 10, Rm B09, Bethesda, MD, 20205

Cancer Treat Rep; 65(9):739-746 1981

We have studied gonadal function in five patients (3 men and 2 women) who received high-dose methotrexate (HD-MTX) alone and in 12 patients (7 men and 5 women) who received HD-MTX and vincristine (VCR) as postoperative adjuvant therapy for osteosarcoma. Testicular function was assessed by determination of testicular size, sperm concentration, and serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone levels while evaluation of ovarian function was based on menstrual history and serum FSH, LH, estradiol, and progesterone levels. The two women who received HD-MTX and all five women who received HD-MTX and VCR had regular cyclic menses not only after therapy but also during treatment. Serum FSH, LH, estradiol, and progesterone levels were normal in all women studied. Among the 10 men studied, testicular function was normal in the 6 patients evaluated initially several mo after the completion of therapy. In contrast, severe oligospermia was noted among four men evaluated during and immediately after treatment. From serum samples obtained before, during, and after treatment we have determined that approx one half of the men who received HD-MTX alone or in combination with VCR develop transient testicular failure associated with a significant increase in serum FSH but not LH levels. Sperm concentration and serum FSH levels then return to normal after completion of chemotherapy. (Author abstract) (46 Refs)

29. SOME ASPECTS OF PITUITARY FUNCTION AFTER NEUROADENOLYSIS IN PATIENTS WITH METASTATIC CANCER.

Deshpande N, Morrica G, Saullo F, Di Martino L, Kwa G

Imperial Cancer Res. Fund, Lincoln's Inn Field, London W.C. 2 A 3 PX, England

Tumori; 67(4):355-359 1981

The effects of neuroadenolysis on plasma titers of beta-endorphin, beta-lipotropin, ACTH, TSH and prolactin have been investigated in five patients with metastatic cancer who responded to the treatment and have been in remission for more than 4 yr and in five others who were undergoing the treatment for the first time for pain due to cancer metastases. Beta-endorphin, beta-lipotropin and ACTH titers were within the normal ranges of values in both categories of patients but post-neuroadenolysis titers of these peptides were higher than those before the treatment. The ability to secrete TSH and prolactin and to respond to thyroid stimulating hormone releasing hormone (TRH) remains intact following the treatment. However, whereas basal TSH titers and response to TRH was lower in the majority of patients, no such effect was observed on prolactin secretion. Plasma titers of prolactin and TSH were below the sensitivity of the method in the five patients who are in remission for more than 4 yr. These preliminary findings suggest that neuroadenolysis probably affects some mechanism(s) associated with the control of beta-endorphin, beta-lipotropin and ACTH synthesis. (Author abstract) (18 Refs)

30. HYPERCALCEMIA COMPLICATING SMALL-CELL CARCINOMA.

Hayward ML, Howell DA, O'Donnell JF, Maurer LH
Hitchcock Clinic, Hanover, NH, 03755
Cancer; 48(7):1643-1646 1981

Hypercalcemia is a common paraneoplastic syndrome complicating some varieties of lung cancer. It has rarely been reported with small-cell carcinoma of the lung. Seven cases of hypercalcemia complicating small-cell carcinoma of the lung are described; clinical features indicate that significant bone or bone marrow involvement is present in all cases. Parathormone assays were found to be generally in the normal range, though inappropriate for the level of hypercalcemia. (Author abstract) (17 Refs)

31. UNSUSPECTED HYPERCALCEMIA AMONG ADULTS IN HOSPITAL.

Finnis WA, Cohanim M, Yendt ER
(c/o Yendt) Etherington Hall, 102 Stuart St., Kingston, Ontario K7L 2V6, Canada
Can Med Assoc J; 125(6):561-564 1981

Unsuspected hypercalcemia was identified in 173/12,000 hospital patients admitted during a 1-yr period. The hypercalcemia was overlooked by the attending physician in 131 cases, including 21 patients with malignant disease and 21 with hyperparathyroidism. Serum calcium levels in these patients are discussed. (15 Refs)

32. PARENTERAL DIPHOSPHONATES FOR TREATING MALIGNANT HYPERCALCEMIA.

Jung A, Van Ouwenaller C, Chantraine A, Courvoisier B
Clinique Medicale Therapeutique, Hopital Cantonal Universitaire, 1211 Geneva, Switzerland
Cancer; 48(8):1922-1925 1981

Two diphosphonates, EHDP (disodium etidronate, or ethanehydroxy-diphosphonate) and Cl2MDP (disodium clodronate, or dichloromethylene-diphosphonate) were injected in various doses in six patien with one or multiple episodes of malignant hypercalcemia. All patients responded well to the drugs after a delay period of 2 to 7 days. The tolerance of the drugs was excellent. EHDP, and especially Cl2MDP, are promising agents for treating hypercalcemia and inhibiting bone resorption in malignant disorders. (Author abstract) (13 Refs)

33. SOMATOSTATIN, GASTROINTESTINAL PEPTIDES, AND THE CARCINOID SYNDROME.

Long RG, Peters JR, Bloom SR, Brown MR, Vale W, Rivier JE, Grahame-Smith DG
Gastrointestinal Lab., St. Thomas' Hosp., London SE1 7EH, England
Gut; 22(7):549-553 1981

During a control infusion noradrenaline and alcohol each provoked carcinoid flushing in four of five patients and pentagastrin in two of five patients. When tetradecapeptide somatostatin was infused on another day no patient flushed at any time, even when 16 ug of either noradrenaline or pentagastrin were administered. Carcinoid flushing was not associated with release of gastrin or any of the other vasoactive or postprandially released gut regulatory peptides measured. In a sixth patient with severe prolonged carcinoid flushing, sc Des AA1,2,4,5,12DTrp8 somatostatin markedly reduced the incidence and severity of flushing for 2 days. Somatostatin is thus a potent inhibitor of carcinoid flushing, but no evidence has been found for the gut hormones measured to be mediators of flushing. (Author abstract) (21 Refs)

34. RESEARCH ON SERUM MELATONIN: AGE-DEPENDENT CHANGES IN SERUM MELATONIN CONCENTRATIONS IN HEALTHY HUMAN SUBJECTS AND IN PATIENTS WITH ENDOCRINE AND HEPATIC DISORDERS AND RENAL FAILURE.

Iguchi H

Third Dept. Internal Medicine, Kyushu Univ. Faculty Medicine, Fukuoka 812, Japan

Fukuoka Igaku Zasshi; 72(7):423-430 1981

Changes in serum melatonin concentrations were measured with a radioimmunoassay method in 81 healthy subjects (44 men, 37 women; 1-92 yr old) and in 98 patients (15-61 yr old) with endocrine disorders, hepatic diseases, and renal failure. The patients included four with non-functioning pituitary adenomas, four with pinealomas, four with Cushing's syndrome, and two with pheochromocytomas. The mean daytime serum level of melatonin in the healthy subjects was 5.5 +-0.4 picog(pg)/ml, and the daytime serum levels decreased with advancing age. Nocturnal elevation of serum melatonin levels was diminished in the aged group of healthy subjects as compared to the younger subjects. Compared to the healthy subjects, the patients with pituitary disorders, pinealomas, thyroid dysfunction, adrenal diseases, and chronic renal failure showed no significant fluctuations in daytime serum levels of melatonin, but daytime serum levels of melatonin were elevated in patients with liver cirrhosis and acute hepatitis. (29 Refs) (In JPN)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

35. EFFECT OF BROMOCRIPTINE, SOMATOSTATIN, AND OESTRADIOL-17BETA ON HORMONE SECRETION AND ULTRASTRUCTURE OF HUMAN PITUITARY TUMOURS IN VITRO.

Prysor-Jones RA, Kennedy SJ, O'Sullivan JP, Jenkins JS

Dept. Medicine, St. George's Hosp. Medical Sch., London, SW17 ORE, England

Acta Endocrinol (Copenh); 98(1):14-23 1981

The effect of bromocriptine and somatostatin on hormone secretion and the ultrastructure of human pituitary adenomas was studied in vitro. Prolactin secretion was inhibited by bromocriptine in 3 out of 10 prolactin-secreting tumors and in explants from two normal pituitaries. GH secretion was reduced by bromocriptine in four out of six GH-secreting adenomas but was not affected by the drug in the incubations of normal pituitaries. Somatostatin inhibited GH secretion in two out of five pituitary adenomas and the effect was comparable with that of bromocriptine. Incubation of prolactin-secreting adenomas with estradiol for a long as 24 days produced no change in hormone secretion. Examination of tumor explants by electron microscopy showed that somatostatin and bromocriptine produced accumulation of secretion granules but no changes in the secretory organelles. Long term bromocriptine treatment of 'nude' athymic mice bearing xenografts of human pituitary adenomas suppressed hormone secretion and produced some increase in secretion granules but there were no morphological changes in the secretory organelles or other vital structures of the adenoma cells. (Author abstract) (27 Refs)

36. MULTIPLE FORMS OF GROWTH HORMONE: DETECTION IN MEDIUM FROM CULTURED PITUITARY ADENOMA EXPLANTS.

Talamantes F, Lopez J, Lewis UJ, Wilson CB
Div. Natural Sciences, Thimann Lab., Univ. California Santa Cruz, Santa Cruz, CA, 95064
Acta Endocrinol (Copenh); 98(1):8-13 1981

Three pituitary adenomas obtained from patients with acromegaly were maintained in organ explant culture for a period of 12 days in a defined culture medium. Lyophilized culture medium from each was then examined by electrophoresis to determine which forms of growth hormone were secreted by the explants. All three explants secreted principally the major form of growth hormone. One adenoma however secreted unusually large amounts of two slowly migrating forms which were in low concentration in the GH-containing granules of normal pituitaries. On the other hand the adenoma produced a much lower amount of a 20,000-dalton variant than was seen in normal pituitary glands. The other two adenomas did not secrete the relatively large amounts of the slowly migrating forms although the quantity of the 20,000-dalton form was less than the amount seen in the normal pituitary. There was no evidence of proteolytic alteration of the growth hormone during the culturing process. In companion experiments with rat pituitary glands the growth hormone did not undergo proteolytic degradation in the gland left in situ for 96 hr at 5 C. (Author abstract) (16 Refs)

37. RESTORATION OF PITUITARY PROLACTIN SYNTHESIS AND RELEASE BY THE ADMINISTRATION OF MORPHINE TO RATS BEARING A TRANSPLANTED PROLACTIN-SECRETING TUMOR.

Login IS, Nagy I, MacLeod RM
Dept. Neurology, Box 394, Univ. Virginia Sch. Medicine, Charlottesville, VA, 229 08
Neuroendocrinology; 33(2):101-104 1981

Morphine sulfate (MS: 1.44 mg/day) and haloperidol (HP: 0.11 mg/day) were tested for their effects on pituitary prolactin (PRL) synthesis in female Wistar-Furth rats implanted with a PRL-secreting pituitary tumor (MtTW15). Anterior pituitary glands from untreated tumor-bearing rats incorporated 3H-leucine into newly synthesized 3H-PRL equivalent to 1,687 cpm/mg pituitary; of this amount, 657 cpm/mg was synthesized and released into the incubation medium. Constant infusion of MS or HP for 4 days using an osmotic pump caused a significant increase in synthesis (p less than 0.01) and release (p less than 0.01) of PRL. Pituitary glands from HP-treated rats had 3H-PRL synthesis and release rates equivalent to 5,870 and 2,487 cmp/mg, respectively; the corresponding values for MS-treated rats were 3,307 and 1,558 cmp/mg, respectively. HP, but not MS, treatment resulted in a significant increase in serum PRL levels. Probable mechanisms by which HP and MS affected pituitary hormone synthesis are discussed. (14 Refs)

38. INSULIN SECRETION BY A TRANSPLANTABLE RAT ISLET CELL TUMOUR.

Sopwith AM, Hutton JC, Naber SP, Chick WL, Hales CN
Dept. Clinical Biochemistry, Univ. Cambridge, Addenbrooke's Hosp., Hills Rd., Cambridge CB2 2QR, England
Diabetologia; 21(3):224-229 1981

A transplantable rat islet cell tumor was studied as a possible large-scale model for insulin secretion. Stimulation and inhibition of insulin secretion by various agents were examined. Glucose (8.4-48 mM) did not stimulate secretion. Increased release of insulin was provoked by leucine (max response at 20 mM) and theophylline (max response at 5mM). Leucine and theophylline in combination produced a greater-than-additive effect. Insulin release was also stimulated by dibutyryl cyclic AMP. Presence of glucose, pyruvate, glutamate, and fumarate in the buffer resulted in accelerated response to stimulation. Insulin release was inhibited by sodium cyanide (1 mM), antimycin A (5 uM), 2,4-dinitrophenol (0.3 mM), and the presence of lanthanum, magnesium, or cobaltous ions, adrenalin, calmodulin, and somatostatin. Insulin release by islet cell tumor was thus shown to occur in response to specific stimuli and to depend on the cellular energy system. It apparently occurs by an exocytotic process similar to that occurring in normal islet cells; the tumor may therefore be used as a model for the insulin secretory process. (39 Refs)

39. THE EFFECTS OF IONIZING RADIATION AND OESTROGEN TREATMENT ON THE STEROID-RECEPTOR CONCENTRATIONS IN EXPERIMENTAL MAMMARY CARCINOMA.

Janssens JP, Wittevrongel C, Van Dam J, Goddeeris P, Lauwerijns JM, De Loecker M
Dept. Biochemistry, Faculty Medicine, Univ. Louvain, B-3000 Leuven, Belgium
Biochem Soc Trans; 9(1):95-96 1981

Mammary carcinoma was induced in Sprague-Dawley rats by intragastric injection of 7,12-dimethylbenz[a]anthracene. Tumors appeared after 3 mo. Some rats were irradiated with 20 Gray from a cobalt teletherapy source. Some were treated for three days by sc injection of 5 ug 17beta-estradiol (EDB). Controls remained untreated. Steroid receptor concentrations were determined 40 hr after final hormone treatment or up to 65 days after irradiation. Tumor regression to 25% of pretreatment size occurred during the first 30 days after irradiation. Renewed growth followed, reaching 90% of the pretreatment size by 65 days. EDB-receptor concentrations fell from 2.56 femtomoles/mg (fm/mg) to 1.09 fm/mg during the first 30 days. They remained at the low level during tumor regrowth. Progesterone-receptor levels fell from a control level of 7.39 fm/mg to 1.83 fm/mg during tumor regression and increased during tumor regrowth to 2.36 fm/mg at 65 days. EDB treatment at 65 days restored progesterone-receptor levels to normal control values. EDB-receptor concentrations were not affected by EDB treatment. Evidently the EDB-receptor system, which is necessary for the stimulation of the progesterone-receptor system, remains intact and active after irradiation, although the concentration of receptors is reduced. Interpretation of receptor concentrations measured during endocrine and radiation therapy should be made as a function of these factors. (9 Refs)

40. NEW ASPECTS IN THE DEVELOPMENT OF CYTOTOXIC-LINKED ESTROGENS FOR THE CONTROL OF BREAST NEOPLASIA.

Leclercq G
Laboratoire de Cancerologie mammaire, Service de Medecine, Institut J. Bordet, 1000 Brussels, Belgium
Arch Geschwulstforsch; 51(7):643-649 1981

The selection and use of cytotoxic-linked estrogens, which bind to estrogen receptors (ERs) and thereby specifically concentrate in the target tissues including breast neoplasms, are described. The selection of these agents is based upon their binding ability to cytoplasmic ERs, their cytotoxicity against two human breast cancer cell lines (ER+ MCF-7 and ER- Evas-

T), and their endocrinologic properties and toxicology. Four epoxide derivatives of 17-beta-estradiol and 17-alpha-estradiol were found to reversibly bind with ER but showed no cytotoxicity against MCF-7 and Evsa-7 cell lines. Nitrogen mustard derivatives of hexestrol, diethylstilbestrol, and estrone displayed binding affinity for ER and cytotoxicity against MCF-7 cells. Only the two mononitrogen mustard derivatives of estrone inhibited growth of Evsa-7 cells. This indicated that these nitrogen mustard derivatives had a weaker effect on the Evsa cell line, consistent with the hypothesis of a participation of ERs in their cytotoxic action. The results indicated that the linking of a cytotoxic group on an estrogen in an appropriate position can yield a drug with a significant binding affinity for ERs. The therapeutic implications of these findings are discussed. (13 Refs)

41. MELATONIN INHIBITION AND PINEALECTOMY ENHANCEMENT OF 7,12-DIMETHYLBENZ(A)ANTHRACENE-INDUCED MAMMARY TUMORS IN THE RAT.

Tamarkin L, Cohen M, Roselle D, Reichert C, Lippman M, Chabner B
Intramural Res. Program, Natl. Inst. Child Health and Human Development, NCI, NIH, Bethesda, MD, 20205
Cancer Res; 41(11,part1):4432-4436 1981

The effects of the pineal hormone, melatonin, and of pinealectomy on the incidence of mammary adenocarcinoma in Sprague-Dawley rats treated with 7,12-dimethylbenz(alpha)anthracene (DMBA) were investigated. Melatonin (2.5 mg/kg), begun on the same day as DMBA (15 mg) treatment and given daily in the afternoon for 90 days, significantly reduced the incidence of mammary tumors from 79% (control) to 20% (treated) (p less than 0.002). Rats pinealectomized at 20 days of age and treated with 7 mg of DMBA at 50 days of age had a lighter incidence of tumors (88%) compared to control animals (22%). Fifteen mg of DMBA, which resulted in a higher incidence of tumors, reduced the difference between pinealectomized and control animals. Melatonin only partially reversed the effects of pinealectomy, reducing the incidence from 87% (pinealectomy alone) to 63% (pinealectomy plus melatonin); however, the tumor incidence was still lower (27%) in nonpinealectomized, melatonin-treated animals. Assessment of plasma prolactin, luteinizing hormone, follicle-stimulating hormone, estradiol, and cortisol in DMBA-treated tumor-free and tumor-bearing animals revealed a significantly lower plasma prolactin concentration [27 +-5 (SE)ng/ml] in melatonin-treated animals as compared to vehicle-treated animals [65 +-8 ng/ml]. The concentration of plasma prolactin was less in melatonin-treated, pinealectomized rats (55 +-10 ng/ml) as compared to vehicle-treated, pinealectomized animals (101 +-13 ng/ml). Other hormones were not affected by melatonin treatment. These data support the hypothesis that melatonin inhibits the development of DMBA-induced mammary tumors in the rat while removal of the pineal gland stimulates development of such tumors. Additionally, these experiments provide evidence that these effects may be mediated by a suppression of plasma prolactin levels. (Author abstract) (28 Refs)

42. ESTROGENIC EFFECTS OF PHYSIOLOGICAL CONCENTRATIONS OF 5-ANDROSTENE-3BETA,17BETA-DIOL AND ITS METABOLISM IN MCF7 HUMAN BREAST CANCER CELLS.

Adams J, Garcia M, Rochefort H
Unite d'Endocrinologie Cellulaire Moleculaire, U 148 INSERM, 60, Rue de Navacelles, 34100 Montpellier, France
Cancer Res; 41(11,part1):4720-4726 1981

The compound 5-androstene-3beta,17beta-diol (ADIOL) has previously been shown to have a high affinity for the estrogen receptor and to translocate it to the nucleus in vitro and in vivo. This compound and related C19 delta5-steroids of adrenal origin have now been examined for their ability to induce the synthesis in MCF7 cells of an estrogen-dependent secreted glycoprotein (mol wt 46,000). Concentrations required for half-max induction were 2 nM for ADIOL and 500 nM for dehydroepiandrosterone (DHEA). Dehydroepiandrosterone sulfate showed weak inducing ability at concentrations of 1 uM or greater. The induction by ADIOL was unaffected by the presence of an aromatase inhibitor, and 5alpha-androstane-3beta,17beta-diol, which cannot be aromatized, also induced the mol wt 46,000 protein at low concentrations. When cells were exposed to 10 nM [3H]ADIOL, the cytosol and nuclear fractions contained [3H]ADIOL resistant to charcoal adsorption. The bound [3H]ADIOL in the cytosol and nucleus was displaceable by 17beta-estradiol and tamoxifen, suggesting that it was binding to the estrogen receptor. [3H]ADIOL was metabolized to its 3beta-sulfate, which was excreted into the medium, and to [3H]DHEA, which was found in the cells and the medium as free DHEA and its 3beta-sulfate. [3H]DHEA was also metabolized by the cells to its 3beta-sulfate, to free ADIOL, and to the 3beta-sulfate of ADIOL. We conclude that: (a) ADIOL is effective as an estrogen in MCF7 cells at a concentration of 2 nM, which is within the range found in the blood of normal women; and (b) sulfurylation is a major route of inactivation of 3beta-hydroxy delta5-steroids in MCF7 cells. (Author abstract) (31 Refs)

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HE 20. 3173/2:

PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. SOME PITFALLS IN THE DIAGNOSIS OF PITUITARY TUMOURS: THE IMPORTANCE OF CAROTID ANGIOGRAPHY.

Khangure MS, ApSimon HT
(c/o ApSimon), Royal Perth Hosp., Post Office Box X2213, Perth 6001, Australia
Surg Neurol; 16(4):300-308 1981

Headache and the radiological finding of an abnormal pituitary fossa are a frequent mode of presentation in patients with pituitary tumors. The case histories and radiological findings of four patients who presented with the above features, and in whom the major abnormalities of the pituitary fossa were due mainly to variations in the cavernous portions of the carotid artery, are described. The role of carotid angiography in the investigation of a patient with an abnormal pituitary fossa is stressed. (Author abstract) (29 Refs)

2. GAS CISTERNOGRAPHY ('MINIGAS') FOR PREOPERATIVE AND PEROPERATIVE EVALUATION OF PITUITARY ADENOMAS (MEETING ABSTRACT).

Eldevik OP
Neuroradiological Department, Ulleval Hospital, Oslo, Norway
Acta Neurochir; 56(1/2):120 1981

From October 1978 to May 1980 45 patients with pituitary tumors have been operated on transnasally at our hospital. The preoperative neuroradiological work-up of these patients consisted of skull films, computed tomography, gas cisternography and angiography, in this order. Preoperative gas cisternography was done on a polytomography table with fluoroscopy. A lateral C1-C2 puncture with gauge 22 spinal needle was performed under fluoroscopic control. Then 5 to 15 ml oxygen was insufflated, filling the prepontine and suprasellar cisterns. Lateral and frontal tomograms of the sella, sphenoidal sinus, and posterior nasal cavity were obtained. A good visualization of the suprasellar cistern with possible suprasellar growth of the pituitary tumor was obtained as well as thin-section tomograms of the sella and sphenoidal sinus. Preoperative gas cisternography was performed by the neuroradiologist in the operating room with lateral fluoroscopy of the sellar region during the operation. A lateral C1-C2 puncture was performed, and the needle was left in place during the operation for refill of gas. We used 3-5ml gas at a time, up to a total of 30 ml. During the neurosurgical evacuation of the pituitary tumor the neuroradiologist was present in the operating room using fluoroscopy of the gas-filled cisterns to guide the neurosurgeon and reduce the risk of this critical part of the operation. (no Refs)

3. RADIOLOGIC EXAMINATION PITUITARY ADENOMAS (MEETING ABSTRACT).

Johansson I, Radberg C
Radiodiagnostic Department, University Hospital, Linkoping, Sweden
Acta Neurochir; 56(1/2):115 1981

The primary radiological examination in pituitary adenomas has been plain films of the sella turcica. Gross changes of the sella are obvious on plain films, but small alterations of the shape and subtle erosions are recognized only if several projections or multidirectional tomograms of the sella are obtained. Plain films are followed by computed tomographic (CT) scan-including iv contrast enhancement-to determine possible extrasellar extension of the adenoma or intrasellar herniation of the suprasellar cisterns. For more precise definition of the suprasellar area pneumoencephalography including tomography has been performed in patients with CT proven suprasellar tumor. Metrizamide cisternography has been used only exceptionally. Carotid angiography has been employed when skeletal changes or CT scan indicate parasellar extension, and to exclude an arterial aneurysm or aberrant course of the internal carotid artery. Phlebography has been applied in some few cases to demonstrate cavernous tumor extension when transsphenoidal approach is contemplated. Preoperatively before a transsphenoidal operation the anatomy of the sphenoidal sinus is always analyzed with the aid of tomograms in the AP projection. (no Refs)

4. HISTOPATHOLOGY IN PITUITARY ADENOMAS: PROBLEMS IN ROUTINE EXAMINATION (MEETING ABSTRACT).

Enestrom S
Department of Pathology, University Hospital, Linkoping, Sweden
Acta Neurochir; 56(1/2):116 1981

Thirty-nine cases of pituitary adenomas removed by transsphenoidal surgery have been evaluated by light microscopy according to the amount of chromophilic granules. Only a slight correlation between the occurrence of acidophilic granules and human growth hormone or prolactin (PRL) hyperfunction could be found. An immunofluorescence method for detection of PRL containing cells must be used to reveal the prolactinomas. The classic concept of pituitary adenomas consisting of chromophobe, acidophilic, or basophilic lesions is thus not well adapted to the functional classification of these tumors. There seems to be no simple relationship between the cell types and the hormone secretion as based on the traditional staining methods. Until immunocytochemical classification of pituitary adenomas has been adopted the diagnosis must rest on clinical findings. (no Refs)

5. IMMUNOCYTOCHEMICAL CLASSIFICATION OF PITUITARY ADENOMAS (MEETING ABSTRACT).

Attramadal A, Nesbakken R, Torjesen PA
Institute of Pathology, Rikshospitalet, Oslo, Norway
Acta Neurochir; 56(1/2):122 1981

Studies of pituitary adenomas have clearly shown that classification of these tumors, based on granule staining properties, into acidophil, basophil, and chromophobe has outlived its usefulness. Functional classification based on the hormones secreted seems to be more informative. We have used an immunocytochemical method for identification of the hormones produced by by the adenoma cells. The specificity and sensitivity of this technique appear appropriate for accurate assessment of the functional status of pituitary adenomas and for functional classification. Biopsy specimens from human pituitary adenomas were examined for the hormones produced by the immunoperoxidase (PAP) technique using high titre antisera. In order to assess the validity of functional classification based on this method, the results were correlated with corresponding levels of circulating hormones measured preoperatively by radioimmunoassay. Forty-two human pituitary adenomas were examined. Twenty of the tumors showed on ly or mainly prolactin producing cells whereas 12 were exclusively or predominantly composed of cells containing growth hormone. One tumor possessed exclusively cells with thyroid stimulating hormone. Four of the tumors displayed about equal amounts of growth hormone and prolactin producing cells, while twelve more tumors showed scattered cells with hormone production diffferent from that of the main type. Prolactin and growth hormone were the hormones mostly involved. In six of the tumors no hormone producing cells were detectable. The immunocytochemical results correlated excellently with the levels of circulating hormones measured preoperatively. (no Refs)

6. IMMUNOHISTOCHEMICAL STUDIES ON FUNCTIONING PITUITARY ADENOMAS (MEETING ABSTRACT).

Teramoto A, Sano K

Department of Neurosurgery, University of Tokyo Hospital, Tokyo, Japan

Acta Neurochir; 56(1/2):123 1981

In an attempt to establish the immunohistochemical classifications of functioning pituitary adenomas, 37 prolactin (PRL) producing, 40 growth hormone (GH) producing, and 13 ACTH producing adenomas were studied by the peroxidase labelled antibody method. 1) PRL producing adenomas: With hematoxylin-eosin (HE) and PAS-orange G stains, all the tumors were classified as chromophobe adenomas except for two, which were acidophilic. Immunohistochemically, PRL producing adenomas were classified into two types according to the population of PRL cells and the intracytoplasmic localization of immunoreactive PRL. 2) GH producing adenomas: With HE and PAS-orange G stains, these were classified as acidophilic, chromophobe, and mixed adenomas. Immunohistochemically, GH producing adenomas were also divided into two groups according to the population of GH cells (Diffuse type, Sporadic type). In either type of adenoma, GH cells were round to polygonal in shape, with immunoreactive GH throughout the cytoplasm. Clinically both types of adenoma were distributed from microadenomas to large ones, whereas the former type showed higher serum GH levels than the latter. 3) ACTH producing adenomas: of 13 cases, seven adenomas were associated with Cushing syndrome, and six with Nelson syndrome. With conventional stains, four cases were basophilic, possessing PAS positive granules, while others were composed of chromophobic cells. With immunostains, all of them showed diffuse staining for ACTH, whereas Crook's cells were found only in the cases of Cushing disease. (no Refs)

7. MASSIVE CROOKE'S HYALINIZATION IN CORTICOTROPH CELL ADENOMAS OF THE HUMAN PITUITARY: A HISTOLOGICAL, IMMUNOCYTOLOGICAL, AND ELECTRON MICROSCOPIC STUDY OF THREE CASES.

Felix IA, Horvath E, Kovacs K

Dept. Pathology, Hosp. '20 de Noviembre' (ISSSTE), av. coyoacan y Felix Cuevas, Colonia del Valle 12, Mexico

Acta Neurochir (Wien); 58(3/4):235-243 1981

Three women with Cushing's disease caused by ACTH-producing adenoma, underwent transsphenoidal tumor resection. Many adenoma cells showed massive accumulation of microfilaments indistinguishable from Crooke's hyaline material by light and electron microscopy. We believe that these tumors represent variants of ACTH-producing adenomas, and the accumulation of microfilaments is due to cortisol dependency. (Author abstract) (22 Refs)

8. IMPARIED PITUITARY RESPONSE TO BROMOCRIPTINE SUPPRESSION: REVERSAL AFTER BROMOCRIPTINE PLUS TAMOXIFEN (MEETING ABSTRACT).

Volker W, Gehring WG, Zur Muhlen AV

Medizinische Hochschule Hannover, Hannover, W. Germany

Acta Endocrinol [Suppl]; 96(240):71 1981

The present study was undertaken on the assumption that bromocriptine plus tamoxifen might have a synergetic effect in previously resistant cases of prolactinoma to bromocriptine monotherapy. Twelve women aged 16 to 54 were tested. Two of them were unable to take bromocriptine because of severe side-effects, the others were under longterm bromocriptine therapy. Nine women had sellar or suprasellar enlargement, five of them having undergone incomplete surgical resection. The others had normal sella tomograms, but suppression was poor or impossible. Ten women continued taking bromocriptine, but additionally received tamoxifen 10 mg bid. Blood samples were taken before the beginning of combined therapy and one of four wk later. Prolactin (PRL), luteinizing hormone, follicle-stimulating hormone, estradiol and progesterone were determined by radioimmunoassay. The two women who had previously been unable to take bromocriptine were able to accept it in conjunction with tamoxifen. The combination with tamoxifen resulted in a marked suppression of PRL in six out of ten patients. In four cases there was no effect at all. In the three women with normal sella, PRL was suppressed to normal values. In the cases with sellar or suprasellar tumors the addition was successful in three, unsuccessful in four. No correlation was found between this effect and the extent of the tumor. In both women who tolerated bromocriptine when tamoxifen was added, PRL was suppressible. One woman conceived shortly after the combined therapy had been started. In six women spontaneous bleedings occurred, only in four of them had PRL been suppressed sufficiently. Basal body temperature curves became normal in three women, galactorrhea ceased in five. One woman reported a marked improvement of libido. The suppressive effect of bromocriptine on PRL secretion is enhanced by addition of tamoxifen in most cases of adenomatous hyperprolactinemia. Side-effects of bromocriptine are considerably improved by tamoxifen. (6 Refs)

9. PITUITARY APOPLEXY IN ACROMEGALY DURING BROMOCRIPTINE THERAPY.

Yamaji T, Ishibashi M, Kosaka K, Fukushima T, Hori T, Manaka S, Sano K

Third Dept. Internal Medicine, Faculty Medicine, Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan

Acta Endocrinol (Copenh); 98(2):171-177 1981

Two cases of pituitary apoplexy occurring in the course of long-term bromocriptine therapy for active acromegaly are described. Although bromocriptine was effective in lowering serum growth hormone levels and concomitant clinical improvement was achieved, both patients developed an acute episode suggesting pituitary apoplexy when the therapy was continued for 6 and 24 mo, respectively. Surgery verified marked hemorrhage and necrosis of an eosinophilic pituitary adenoma in each case. Bromocriptine may have suppressed the growth of these pituitary adenomas resulting in necrosis of the tumor, followed by hemorrhage into the adenoma. Pituitary apoplexy has not been documented as a complication of bromocriptine therapy. This report points out a possible role of bromocriptine in the development of this catastrophe and that careful follow-up is required when long-term treatment with bromocriptine is attempted. (Author abstract) (29 Refs)

10. CALCITONIN-LIKE IMMUNOREACTIVITY IN THE PITUITARY VASCULAR BED OF MAN.

Samaan NA, Leavens ME

Section Endocrinology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030

J Clin Endocrinol Metab; 53(5):985-989 1981

The calcitonin-like immunoreactivity (CT-like immunoreactivity) was measured in blood aspirated from the vascular bed of the anterior pituitary gland during transphenoidal surgery in 33 patients with PRL-producing microadenomas, 2 patients with Cushing's disease, and 1 patient with metastatic breast cancer with a normal pituitary gland. The mean level of CT-like immunoreactivity in the pituitary vascular bed was 2-3x higher than in peripheral blood (2.4 +-0.9 ng/ml vs 0.69 +-0.19 ng/ml), and the difference was highly significant (p less than 0.001). However, the serum ACTH, hCG, TSH, PRL, and FSH in the pituitary vascular bed was 1,000x higher than that found in the peripheral blood. The serum CT-like immunoreactivity levels in the pituitary bed in the two patients with Cushing's disease were similar to that found in other patients. Our investigations indicate (1) CT-like immunoreactivity in man is higher in the blood obtained from the pituitary vascular bed than that found in the peripheral blood; (2) the serum CT-like immunoreactivity level in the pituitary vascular bed is much less than ACTH or the other hormones secreted by the pituitary gland; (3) there is no correlation between CT-like immunoreactivity and ACTH levels. (Author abstract) (23 Refs)

11. GAMMA-MELANOTROPHIN-LIKE IMMUNOREACTIVITIES IN HUMAN PITUITARIES, ACTH-PRODUCING PITUITARY ADENOMAS, AND ECTOPIC ACTH-PRODUCING TUMOURS: EVIDENCE FOR AN ABNORMALITY IN GLYCOSYLATION IN ECTOPIC ACTH-PRODUCING TUMOURS.

Tanaka I, Nakai Y, Nakao K, Oki S, Fukata J, Imura H

Second Div., Dept. Medicine, Kyoto Univ., 54 Shogoin Kawaharacho, Sakyo-ku, Kyoto 606, Japan

Clin Endocrinol (Oxf); 15(4):353-361 1981

Using gel exclusion chromatography on Bio-Gel P-60, gamma-melanotropin-like immunoreactivity (gamma-MSH-LI) in three human pituitary glands, two ACTH-producing pituitary adenomas, and three ectopic ACTH-producing tumors (2 medullary thyroid carcinomas and 1 thymoma) was divided into one or two mol wt classes. The largest component eluted near the position of mouse 16K fragment and was designated big gamma-MSH-LI. This big gamma-MSH-LI was present in all samples. The second one, designated intermediate gamma-MSH-LI, eluted between the position of mouse 16K fragment and human ACTH, and was demonstrated only in two ectopic ACTH-producing tumors. No gamma-MSH-LI emerged at the elution position of synthetic gamma3-MSH. Affinity chromatography on concanavalin A-agarose revealed that a significant fraction (52-68%) of gamma-MSH-LI from human pituitary glands, ACTH-producing pituitary adenomas, and one ectopic ACTH-producing tumor bound to the column and was eluted with alpha-methyl-D-mannopyranoside. In two ectopic ACTH-producing tumors which contained big and intermediate gamma-MSH-LI, a relatively small fraction (27-35%) of gamma-MSH-LI bound to the column and was similarly eluted. These observations suggest that human gamma-MSH-LI is glycosylated and that there is an abnormality in the glycosylation of gamma-MSH-LI in some ectopic ACTH-producing tumors. (Author abstract) (22 Refs)

12. TSH-SECRETING PITUITARY ADENOMAS-MORE FREQUENT THAN HITHERTO RECOGNIZED? (MEETING ABSTRACT).

Nesbakken R, Anderud S

Department of Neurosurgery, Ulleval Hospital, Oslo, Norway

Acta Neurochir; 56(1/2):121 1981

Hyperthyroidism is frequent, but is extremely seldom recognized as being due to hypersecretion of thyroid stimulating hormone (TSH). Only some 15 cases operated on have been reported. Our series of 45 consecutive cases of pituitary 'microadenomas' contains two additional cases, from a population of 4 million inhabitants. Statistically our two patients should not have been found, unless TSH-producing pituitary adenomas are more frequent than hitherto recognized. Some clinical, surgical, and endocrinological details on the two cases were presented. (1 Ref)

13. ENDOCRINE EVALUATION OF PITUITARY ADENOMA TREATMENT (MEETING ABSTRACT).

Karlberg BE, Hjelm H, Nilsson OR, Tegler L

Endocrine Division, Department of Internal Medicine, University Hospital, Linkoping, Sweden

Acta Neurochir; 56(1/2):117 1981

Clinical and biochemical evaluation was performed in about 110 patients treated for pituitary tumors during the last 15 yr at our hospital. After evaluation of clinical symptoms and signs of endocrine dysfunction we have applied a standardized test battery consisting of a stimulation test with 200 ug thyroliberin (TRH) and 100 ug gonadoliberin (LHRH) iv with measurements every 15 min for 120 min of serum concentrations of thyroid-stimulating hormone, prolactin, follicle-stimulating hormone, luteinizing hormone, and, in selected cases, human growth hormone (HGH), and basal concentrations of T4 and T3. Two days later a significant hypoglycemia has been induced by 0.1-0.2 IU insulin/kg body wt iv, and samples have been drawn for analysis of serum concentrations of cortisol, HGH, prolactin, and, in selected cases, ACTH. Seventy-one patients were operated on by the transcranial approach. Thirty-two of these patients had preoperative endocrine insufficiency, and another 11 developed insufficiencies postoperatively, mostly patients with large tumors. Thirty-nine patients were treated by the transsphenoidal approach. They were admitted to surgery mostly for endocrine hyperfunction, which was cured in six patients with acromegaly. Amenorrhea/oligomenorrhea was normalized in 11 out of 16 women, and galactorrhea disappeared in 7 out of 8 patients with prolactinoma, although only 8 out of 20 had normal prolactin concentrations postoperatively. Two of the patients who underwent transsphenoidal operations developed postoperative endocrine deficiencies. In the patients with intrasellar 'microadenomas' the final endocrine assessment can be made six wk after surgery. In about half of the patients with residual elevated concentrations of prolactin, bromocryptine has been given with further improvement of clinical symptoms and decreasing prolactin concentrations. (no Refs)

14. ORAL CONTRACEPTIVE EXPOSURE OF AMENORRHEIC WOMEN WITH AND WITHOUT PROLACTINOMAS.

Jones JR, Kemmann E, Norwood PK
Dept. Obstetrics and Gynecology, CMDNJ-Rutgers Medical Sch., Piscataway, NJ, 08854
Int J Gynaecol Obstet; 19(5):381-387 1981

Extent of prior oral contraceptive (OC) used by women with prolactinomas is compared to that of other women with secondary amenorrhea. Ninety-three of 126 women with secondary hypothalamic-pituitary amenorrhea were evaluated for serum prolactin (PRL), by sella tomography, menstrual history, and OC usage and divided into three groups. Results for 26 patients (Group A) showed prolactinoma and hyperprolactinemia indicated by elevated PRL concentrations (greater than 30 nanog (ng)/ml) and radiographic abnormalities of sella turcica. Results for 26 additional patients (Group B) revealed idiopathic hyperprolactinemia only indicated by PRL levels greater than 30 ng/ml and normal tomographies of the sella. Forty-one patients (Group C) had normoprolactinemia indicated by PRL levels less than 20 ng/ml and normal tomographies of the sella. Duration of OC exposure ranged from none to greater than 12 mo. Evaluation for 'post pill amenorrhea' in OC exposed patients revealed 9, 11, and 15, in Groups A, B, and C, respectively. These proportions were not determined to be significant. The results suggest that nonovulatory patients are likely candidates for OC therapy. Patients with prolactinomas apparently do not differ in the extent of OC exposure from other specified groups of amenorrheic patients. (22 Refs)

15. PRIMARY SUPRASELLAR GERMINOMA (PINEALOMA).

Kinoshita K
Dept. Neurosurgery, Miyazaki Medical Coll., Miyazaki, Japan
Neurol Surg; 9(3):227-239 1981

Historical discoveries and theories of different types of pinealomas, clinical data (such as frequency, sex distinctions, age groups, period from occurrence to diagnosis, symptoms), neuroradiological findings on pinealomas, electroencephalographical findings on pinealomas, medullary fluid parameters related to pinealomas, macroscopic observations of pinealomas, microstructures of pinealomas, relationship to immunology, diagnosis and differential diagnosis of pinealomas, and treatment and results of treatment of pinealomas were discussed. Neuroradiological methods used to detect pinealomas included simple cranial roentgenography, pneumoencephalography, pneumoventriculography, angiography, and computed tomography. High rates of diagnostic certainty of pinealoma was associated with patients 10-20 yr old who have uro-degenerative disease of unknown etiology combined with damage of hypophyseal function and of the optic chiasm. Differences between patients with pinealoma and those with other types of tumors included higher marrow cell counts in pinealoma patients compared to those with craniopharyngiomas, normal hypophyseal function in patients with neurofibromatosis and abnormal function in those with pinealoma, lack of presurgical uro-degenerative disease in patients with hypophyseal tumors, and necrotic changes in the cranial bone of patients with Hand-Schuller-Christian disease who also have uro-degenerative disease. (134 Refs) (In JPN)

16. STEREOTACTIC TREATMENT OF CRANIOPHARYNGIOMAS-15 YEARS' EXPERIENCE (MEETING ABSTRACT).

Backlund EO
Department of Neurosurgery, Karolinska Sjukhuset, Stockholm, Sweden
Acta Neurochir; 56(1/2):125 1981

Since 1966, 96 patients with craniopharyngiomas have been treated at the Department of Neurosurgery, Karolinska Sjukhuset, Stockholm. The consistent aim was to avoid aggressive surgery and, if possible, to use stereotaxic treatment exclusively. So far, 86 have been reviewed, and constitute the present material. Fifty-four were 'primary cases', not treated previously; 39 of these were treated exclusively by sterotaxic methods, in most cases by injection of radionuclide into cysts. In the remaining 15, various therapeutic measures were used in combination. The operative mortality in the whole material of 'primary cases' was zero. Eight patients died during the observation period, four because of recurrent tumor, and four from intercurrent causes. In three of the latter group, only non-vital, insignificant tumor remnants were found at autopsy. Three of the recurrences had very large tumors on admission. Forty-six of the 54 'primary cases' are living at present, the great majority in a perfect condition. Thirty-two patients had recurrent tumor after previous radical surgery ('recurrent cases'). They were referred from other neurosurgeons, who in most instances had regarded the recurrent tumors as inoperable. In 27 stereotaxic treatment was used exclusively; 20 of these are alive, all in a satisfactory state. The total mortality in the 'recurrent case' group was 28; two were operative deaths, and seven patients died later, three because of proved progressive tumor growth. In most instances, the sterotaxic operations have been performed under local anesthesia, and the whole surgical procedure has been characterized by smoothness. Most often, the patient has been able to leave the hospital on the second day after surgery, in sharp contrast to what is commonly seen after more invasive procedures. (no Refs)

17. CRANIOPHARYNGIOMA: EXPERIENCE WITH COMBINED OPERATIVE AND RADIOTHERAPY AND PROBLEMS OF HORMONE SUBSTITUTION.

Resch R, Haas H, Schwarz S, Mayr U, Twerdy K, Huttenberger H
Kinderspital, A-5620 Schwarzach, W. Germany
Dtsch Med Wochenschr; 106(45):1502-1508 1981

Craniopharyngioma, primarily a benign tumor, is associated with a variety of serious problems due to tumor localization. Access to the tumor during surgery is difficult and total resection can rarely be achieved. Growth of the remaining tumor continues and symptoms of increased intracranial pressure, further visual field loss and hormonal disturbances reappear. However, conservative operation in conjunction with radical irradiation shows good results as regards tumor regression and survival with satisfactory quality of life. Irradiation with 50 Gy on av was performed in five out of six children with remaining tumor or tumor recurrence, and satisfactory results were obtained. In all cases tumor size regressed. Endocrine disturbances could be ascertained by the combined LHRH-TRH-insulin test and the clinical picture. In nearly every case there was finally a complete lack of hormones of the pituitary-hypothalamic axis. Substitution of various hormones became necessary in all cases. Meticulous surveillance of children still undergoing developmental maturation is mandatory. All six children are well and lead a nearly normal life. (Author abstract) (25 Refs) (In GER)

THYROID TUMORS

18. ULTRASONOGRAPHY IN THYROID TUMORS: 400 CASES (MEETING ABSTRACT).

Bruneton JN, Drouillard J, Caramella E, Roux P, Occelli JP
No affiliation given
Excerpta Med Int Congr Ser; 547:112 1981

Four hundred patients with a thyroid tumor requiring surgery were seen; all underwent clinical examination, scintigraphy, echography, surgery and histological study. Clinically there were 70 goiters and 330 isolated nodules including 4 instances of adenopathies. All 27 cysts were recognized before surgery and in our opinion echography suffices for diagnosis; scintiscanning does not provide any additional data. All the 70 goiters presented a mixed pattern. As neoplastic degeneration was found in 4 cases, echography like scintigraphy is of little value for presurgical evaluation in these cases. In contrast, echography is the most sensitive technique to detect multiple forms. In our series, there were 70 clinically diffuse lesions; scintiscanning revealed 7 more cases but echography revealed an additional 42 cases while histology diagnosed 135 cases of diffuse lesions. It therefore seems useful for the surgeon to detect by echography if a nodule is isolated or if there are multiple lesions. Among the various 125 hyperechoic nodules seen, there was only one instance of cancer: despite this one occurrence of cancer, observation of hyperechoic nodule would seem to indicate benignity. Observation of a hypoechoic pattern does not allow prediction of its evolution (178 cases with 31 cases of hypoechoic cancer). (no Refs)

19. CLINICAL EVALUATION OF 67GA SCANNING IN THE DIAGNOSIS OF ANAPLASTIC CARCINOMA AND MALIGNANT LYMPHOMA OF THE THYROID.

Higashi T, Ito K, Mimura T, Ohi T, Nishikawa Y, Wilcox JR
Dept. of Radiology, Kanagawa Dental Coll., 82, Inaoka-cho, Yokosuka, Japan
Radiology; 141(2):491-497 1981

While 67Ga uptake has been reported to be highly variable and nonspecific in the diagnosis of malignant tumors of the thyroid, it has also been observed to depend on the histological nature of the lesion. For this reason, the behavior of 67Ga in various types of thyroid cancer was investigated in a prospective study of 86 patients with thyroid masses compatible with anaplastic carcinoma or malignant lymphoma. The study demonstrated a distinct difference in uptake between well-differentiated adenocarcinoma of the thyroid and the more undifferentiated anaplastic carcinoma and malignant lymphoma. (Author abstract) (15 Refs)

20. ROLE OF 131CS SCAN IN PREOPERATIVE DIAGNOSIS OF NONFUNCTIONING THYROID NODULES.

Madeddu G, Casu AR, Tanda F, Costanza C, Dettori G, Arras ML, Langer M
Servizio di Medicina Nucleare, Instituto di Clinica Medica, Viale San Pietro 8, 07100 Sassari, Italy
Am Surg; 47(11):479-482 1981

The role of 131Cs scan in the preoperative diagnosis of cancer was evaluated in 355 patients with either cold or nonfunctioning thyroid nodules. Nodules were classified as positive, doubtful or negative by the pattern or isotope accumulation. Among 234 patients who underwent thyroidectomy, malignant lesions were found in 10.2% of cases. All carcinomas but one found during surgery had been classified as positive by radiocesium scan and were considered as highly suspicious preoperatively; one carcinoma and two papillary adenomas had been classified doubtful and considered presumably malignant. False-positive nodules were found. However, we did not document histologically malignant lesions in nodules which were classified as negative by radiocesium uptake. The routine use of 131Cs scanning may be very useful in patients with cold or nonfunctioning thyroid nodules because of its high sensitivity in excluding malignant lesions. (Author abstract) (21 Refs)

21. THE UTILITY OF FINE NEEDLE ASPIRATION BIOPSY CYTOLOGY IN THE MANAGEMENT OF THYROID TUMORS.

Varhaug JE, Segadal E, Heimann P
Dept. Surgery, Univ. Bergen, Haukeland Sykehus, N-5016 Bergen, Norway
World J Surg; 5(4):573-577 1981

Fine-needle aspiration biopsy as a routine procedure in the preoperative evaluation of thyroid tumors is evaluated in a retrospective study of 264 patients treated by partial or total thyroidectomy for solitary thyroid nodule or dominant nodule in a nontoxic goiter. Fifty-two of the 68 surgically confirmed carcinomas (76%) were diagnosed or suspected on the basis of preoperative fine-needle aspiration cytology. Nine false-negative but no false-positive cytologic diagnoses for carcinoma were made. Nine of 47 cystic tumors were carcinomas, but only 3 of those were suspected preoperatively. Consideration of only the patients having representative biopsy material showed that 85% (52/61) of carcinomas were diagnosed or suspected preoperatively, and 70% (112/160) of benign lesions were diagnosed correctly before surgery. False-negative diagnoses were made in 4.1% of patients with representative biopsies. Fine-needle aspiration biopsy is a useful method for the routine preoperative evaluation of thyroid tumors. (13 Refs)

22. CLINICAL AND HISTOPATHOLOGICAL STUDIES ON MEDULLARY CARCINOMA OF THE THYROID; WITH SPECIAL REFERENCE TO THE DIFFERENCES BETWEEN THE SPORADIC GROUP AND THE FAMILIAL GROUP OF MEDULLARY CARCINOMA.

Tame E, Sahashi K, Akao K, Maeda M, Nimura Y, Hattori T, Iyomasa Y, Yamaguchi A, Miura K
First Dept. Surgery, Nagoya Univ., Sch. Medicine, Showa-ku, Nagoya 466, Japan
Nippon Geka Gakkai Zasshi; 82(5):441-455 1981

A great difference is said to exist in the biological characteristics of the sporadic group and the familial group of medullary carcinoma. However, this matter has not yet been clarified clinically or histopathologically. Therefore six cases of sporadic group and four of familial group medullary carcinoma were studied clinically, histopathologically and electronmicroscopically (especi ally as to secretory granules), while seven cases were studied immunohistochemically with anticalcitonin. In the sporadic group, medullary carcinoma arose unilaterally. Even upon lobectomy or incomplete surgery some patients showed a favorable prognosis, while some had recurrences soon after radical surgery. Except for patients with a favorable prognosis, tumor cells in the sporadic group were mainly atypical. The capsule was incomplete or absent. Infiltration of tumor cells into neighboring thyroid tissue, with strong vascular invasion, was frequently observed. There seemed to be less amyloid and calcification, and lymph node metastasis was severe and frequent. In the familial group, medullary carcinoma arose on both sides multicentrically. After total thyroidectomy, early postoperative recurrence was not observed, and the prognoses were favorable. Tumor cells consisted of typical cells with a varied histological picture. Other histological findings were also generally contrary to those of the sporadic group. Hyperplasia of parafollicular cells was observed in the neighboring thyroid. Accordingly the familial group tumors are considered to be less malignant, on the basis of hyperplasia of parafollicular cells. Secretory granules were numerous in the familial group and few in the sporadic group, but relatively numerous in sporadic cases with favorable prognosis. Therefore the number of secretory granules seems to be related to the grade of malignancy of the tumor. (52 Refs) (In JPN)

23. PREGNANCY AFTER TOTAL THYROIDECTOMY AND 131I THERAPY FOR THYROID CANCER (MEETING ABSTRACT).

Pelizzo MR, Manfe AZ, Casara D, Girelli ME, Busnardo B
University of Padua, Padua, Italy
Eur J Nucl Med; 6:A24 1981

The fear of possible genetic damages usually suggests to avoid pregnancy in patients treated with 131I for thyroid cancer. In our series of more than 400 female patients, subjected to total thyroidectomy and 131I therapy for differentiated thyroid cancer, twelve pregnancies were observed. The age of the patients ranged between 18 and 30 yr; the tumor was papillary in 8 and follicular in 4 cases; neck lymph node metastases were detected in 3 patients, while the other patients were without any metastases. The total dose of 131I ranged from 80 and 360 mCi; the time interval between the last dose and conception was in every case longer than two yr. No patients showed evidence of metastases during pregnancy. They were receiving a suppressive dose of T3 and thyroid stimulating hormone response to thyrotropin releasing hormone was inhibited in all patients when tested before conception. The T3 dose was corrected during pregnancy according to body wt variations. No one showed appreciable side effects during pregnancy which could be referred to T3. Ten pregnancies were regularly carried through and resulted in easy delivery, the other two were both miscarriages of primiparae within the first three mo, no cases of prematurity, congenital anomalies, hypothyroidism or goiter were observed in the offspring. So far no other signs of genetic damages have been observed in the children, the oldest of whom is now 7 yr old. On the basis of these findings, we don't see strong reasons for forbidding pregnancy to patients treated with high doses of 131I, considering also the long life expectancy for young patients with well differentiated thyroid carcinoma. (no Refs)

24. COMPARISON BETWEEN CALCITONIN AND CEA RIA IN THE MANAGEMENT OF MEDULLARY THYROID CARCINOMA (MEETING ABSTRACT).

Girelli ME, Busnardo B, Moro A, Simioni N, Scotton G
No affiliation given
Eur J Nucl Med; 6:71 1981

Serum levels of Calcitonin (CT) and Carcino Embyronic Antigen (CEA), were measured by radioimmunoassay in 35 out of a group of 46 patients with Medullary thyroid carcinoma. Sixteen patients were studied before thyroidectomy, and 19 patients only after treatment. In a total of 29 patients CT and CEA levels were repeatly evaluated by serial blood samples over a 1-4 yr period. Before operation 15 of the 16 patients showed elevated CT levels and only 10 showed elevated CEA levels. After operation 58% of the patients showed elevated CT levels and only 31% elevated CEA levels. No patient neither before nor after thyroidectomy showed elevated CEA with normal CT levels. Significant positive correlation between CT and CEA levels was found. Before operation, patients without metastases seem to have had CT and CEA levels less increased than those of patients with local or distant metastases. The difference becomes more evident after treatment. Of the 16 patients without metastases 5 had persistently elevated CT levels and 2 elevated CEA levels. Of the 12 patients with metastases 10 had elevated CT levels and 7 elevated CEA levels. Persistent elevation of CT levels after thyroidectomy in absence of evident metastases, even though CEA levels are normal, probably reflects the presence of minute occult foci of tumor, primary or metastatic. The data suggest that the production of CEA by MCT is less constant and less sensitive than that of CT, which remains the best marker of Medullary thyroid carcinoma. (no Refs)

25. THYROGLOBULIN LEVELS IN SERA OF PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA. LONGITUDINAL AND CROSS-SECTIONAL STUDIES (MEETING ABSTRACT).

Schatz H, Schroder O, Grebe S
Medizinische Klinik und Poliklinik, Universitat Giessen, Giessen, W. Germany
Acta Endocrinol [Suppl]; 96(240):14 1981

For evaluating the clinical significance of thyroglobulin (TG) measurements in sera of patients with differentiated thyroid carcinoma, longitudinal and cross-sectional studies were performed. A double-antibody radioimmunoassay was used for determination of TG. Serum was taken after withdra wal of thyroxine prior to each I-131 therapy. In all sera, TG antibodies were also determined using a radio-immunoassay (CIS). Whole-body iodine scans were performed after each I-131 therapy. In 15 thyroidectomized patients TG was detectable in the circulating blood. Nine of these patients showed iodine uptake in the neck region. Positive trunk scans were registered in another group, and the highest TG levels of the whole study were measured in this sub-group. In 4 of the 6 cases, TG decreased during the past 2 yr with each I-131 therapy. These changes in TG levels were not always reflected in the scans. In another 15 patients, TG was undetectable at all times of measurement. Whereas both the neck and trunk scans were negative too in 4 patients, positive neck scans were found in 10. In 3 of the 33 patients, TG antibodies were detected so that the numerical results of the TG assay cannot be interpreted. On the other hand, no appearance of TG antibodies was observed in 30 TG-antibody negative patients during the 2 yr. Ten days after I-131 therapy, TG levels were mostly considerably higher than immediately before therapy. TG can be regarded as a tumor marker in cases of differentiated thyroid carcinoma following thyroidectomy. However, its determination can certainly not replace iodine scanning although TG measurement appears to be superior to scanning in some respect: Changes in tumor mass may be sometimes better reflected in TG levels than in conventional iodine scans. A combined application of iodine scanning and TG radioimmunoassay is thus advisable in the follow-up of patients thyroidectomized for differentiated thyroid carcinoma. (no Refs)

26. CHROMOSOME INSTABILITY IN PATIENTS WITH MEDULLARY CARCINOMA OF THE THYROID.

Hsu TC, Pathak S, Samaan N, Hickey RC
M. D. Anderson Hosp. and Tumor Inst., Texas Medical Center, 6723 Bertner Ave., Houston, TX, 77030

JAMA; 246(18):2046-2048 1981

Chromosome analysis in the cultured peripheral blood lymphocytes of multiple endocrine adenomatosis (MEA-II) patients and their siblings demonstrated a preponderance of higher frequency of metaphases with chromosome and chromatid type abnormalities (av, 11.0%) as compared to controls (av, 3.8%). Our preliminary data suggest that MEA-II patients exhibit some degree of chromosome instability. (Author abstract) (8 Refs)

PARATHYROID TUMORS

27. CLINICAL CHARACTERISTICS AND SURGICAL RESULTS IN HYPERPARATHYROIDISM CAUSED BY WATER-CLEAR CELL HYPERPLASIA.

Tisell LE, Hedman I, Hansson G
Kir. Klin. I., Sahlgrenska Sjukhuset, S-413 45 Goteborg, Sweden

World J Surg; 5(4):565-571 1981

The clinical picture and results of surgery in 29 patients (12 women, 17 men) with water-clear cell hyperplasia (WCCH) of the parathyroid gland are evaluated. Characteristics of these patients are compared with those of 531 patients (381 women, 150 men) with single adenoma. Between 1953 and 1978, annual incidence of WCCH did not change, whereas the number of adenoma cases increased markedly. Approx 80% of WCCH patients had serum calcium levels greater than 3 milliM; 70% of adenoma patients had calcium levels less than 3 milliM. A significantly higher proportion of WCCH patients had renal impairment (18/29 vs 102/531). Urolithiasis or renal calcification was present in 21 WCCH patients (72%) and in 313 adenoma patients (59%), but the difference may be explained by a reversed sex ratio (more men than women) among WCCH patients. Bone disease was present in 10 WCCH patients and in 171 adenoma patients. Sixteen WCCH patients vs 114 adenoma patients had mental or neuromuscular symptoms. Hypercalcemia crises occurred in 4 WCCH patients and in 18 adenoma patients. Hyperparathyroidism was surgically cured in 24/29 WCCH patients. Seven of these 24 patients developed hypocalcemia attributable to tissue damage caused by the operative manipulation. Results suggest that normocalcemia can be achieved in most WCCH patients, provided that all parathyroid glands are found and that a remnant corresponding in size to two normal glands is left in place. To reduce the incidence of hypocalcemia after surgery, 150 mg of parathyroid tissue should be left in place. Follow-up showed that all but one patient who had been normocalcemic immediately after surgery remained normocalcemic. Most patients lived 10 yr after surgery; mean survival time of patients who died was 8.5 yr. (27 Refs)

28. PARATHYROID CARCINOMA IN PRIMARY HYPERPARATHYROIDISM. TEST FOR A TUMOR CHARACTERIZATION.

Welter G, Welter HF, Spelsberg F
Abt. fur Radiol. und Nuklearmedizin, Krankenhaus des Bayer.
Kreuzes, Nymphenburger Str. 163, D-8000 Munchen 19, W.
many

ROEFO; 135(3):351-352 1981

Carcinoma of the parathyroid glands (CP) accounts fo
3% of cases of primary hyperthyroidism (pHPT). Of 102
suspected hHPT examined by ultrasonography 2 had CP.
1 had a CP in the lower left lobe of the thyroid and an ad
ma in the lower right lobe. Case 2 had CP in the lower
lobe of the thyroid. The tumors were characterized by a g
ish-white color, firm consistency, thick capsule, and infiltra
of surrounding tissue. Diagnostic criteria for CP include hi
logical and cytological characteristics, regional lymph n
metastases, and remote metastases, primarily in the lung.
enoma is characterized in sonography by a lower echo den
than surrounding thyroid parenchyma, with a nodular conto
Carcinoma is characterized by low echo density and a hi
density, nodular emphasis of the edge contour. Sonographic
agnosis of CP should only be made in combination with cl
cal indications such as high levels of parathormone and rec
rence of pHPT combined with paresis of the recurrent nerv
(6 Refs) (In GER)

ADRENAL TUMORS

29. COMPUTED TOMOGRAPHY OF THE ADRENAL GLAND.

Hattery RR, Sheedy PF, Stephens DH, Van Heerden JA
Dept. Diagnostic Radiology, Mayo Clinic, 200 First St., S. W., Roc
ester, MN, 55901

Semin Roentgenol; 16(4):290-300 1981

Computed tomography (CT) analysis of the adrenal gland i
reviewed and illustrated. Topics presented include anatomy
technique, adrenal tumors (stromal tumors: adrenal cysts, mye
lolipoma; medullary tumors: ganglioneuroblastoma-neuroblas
toma, pheochromocytoma; nonfunctioning cortical tumors: ad
enoma, adenocarcinoma; functioning cortical tumors: Cushing
syndrome, adrenogenital syndrome, feminizing syndrome
mixed syndrome, primary aldosteronism [Conn syndrome], metastasis) and adrenal screening. During the period 1976-1980
approx 3% of 15,000 patients referred for CT body scans had
suspected adrenal pathology. Of these, more than half had
positive CT scan and showed a spectrum of adrenal pathology; tumors were 8% stromal (5% cyst, 3% lipoma or myelolipoma), 27% medullary (5% ganglioneuroblastoma or neuroblastoma, 22% pheochromocytoma), 48% cortical (8% carcinoma, 14% hyperplasia, 26% adenoma: 40% nonfunctioning, 40% aldosteronism, 20% Cushing syndrome), and 17% metastatic. CT adrenal scanning appears to be the most accurate noninvasive imaging procedure available for evaluation of the adrenal glands. (30 Refs)

30. ULTRASOUND DIAGNOSIS OF ADRENAL TUMORS.

Tenbieg W, Gladisch R, Franzen G

Med. Klinik II der Stadt. Kliniken, Grafenstrasse 9, D-6100 Darmstadt, W. Germany

Med Welt; 32(35):1268-1272 1981

Ultrasound diagnosis of adrenal tumors is discussed based on findings in 16 clinical cases. The kidneys and pararenal regions were examined ventrolaterally from right and left sides. The liver and pancreas were used as acoustic windows. Examination while the patient held a deep breath prevented obstruction of scan by the ribs. Tumors found included five pheochromocytomas (PCC), one cortical adenoma, one cortical carcinoma, six adrenal metastases, and three metastases in the adrenal region. Tumor types were distinguished by different sound reflection patterns. PCC was characterized by a rounded form, smooth boundaries, and homogeneous echo border. Symptoms of PCC included headache, tachycardia, sweating, nervousness, tremors, lethargy, and stomach aches. Using real-time sonography tumors of at least 2 cm diameter could be detected. Ultrasonography has the advantage of being noninvasive. It can detect tumors not detectable by methods such as angiography and computer tomography. Preferred diagnostic methods vary with tumor type, location, and stage. (20 Refs) (In GER)

31. AN UNUSUAL CASE OF PRIMARY ALDOSTERONISM DUE TO ADRENAL ADENOMA AND WITH ELEVATED PLASMA RENIN ACTIVITY (MEETING ABSTRACT).

Mittelstaedt GV, Vecsei P, Hackenthal E, Georgi M, Haack D, Filser T, LichtwaldK

Klinikum Mannheim, Mannheim, W. Germany

Acta Endocrinol [Suppl]; 96(240):57 1981

A 46-yr-old female patient with hypertension and low normal serum potassium showed elevated plasma aldosterone concentrations and also elevated plasma renin activities (PRA). The aldosterone concentrations were: 25.1/111.4; 52.2/137.5; 46.1/84.6 ng/100 ml. The corresponding PRA were: 5.0/9.2; 7.8/12.4; 3.4/6.2 ng angiotensin/ml/60 min. The first value was obtained in supine position, the second one after 30 min orthostasis. The normal ranges for aldosterone are 2-10/5-25 ng/100 ml and for PRA 0.3-2.0/0.5-4.0 ng angiotensin/ml/60 min. The plasma cortisol and urinary cortisol metabolites were found normal. Plasma corticosterone was periodically elevated: 1.29; 2.30; 6.64; 5.54; 1.60 ug/100 ml. The plasma deoxycholate was elevated: 136.9; 101.8 ng/100 ml. Unexpectedly, urinary aldosterone-18-glucuronide, free aldosterone and free 18-OH-corticosterone were in the normal range. The catecholamines were also within the normal range. Sonography, isotope nephrography, iv pyelography as well as blood and urine analyses, and the renal venous PRA-quotient did not indicate renal involvement. However, an adrenal adenoma (left side) could be established by computer tomography and phlebography. In the right adrenal venous plasma aldosterone concentration was 930 ng/100ml, in the left one 17,000 ng/100 ml. After removal of the adrenal adenoma, blood pressure, plasma aldosterone, and PRA normalized: 130/90, 120/80 mmHg blood pressure; 9.9/13.7; 4.5/7.1 ng/100 ml plasma aldosterone concentration; 1.7/3.8; 1.1/2.0 ng angiotensin/ml/60 min PRA. This case shows that elevated PRA cannot exclude hypertension with hyperaldosteronism due to an adrenal tumor. The mechanism of the elevation of the PRA is still unknown. (no Refs)

32. A SCREENING TEST TO IDENTIFY ALDOSTERONE-PRODUCING ADENOMA BY MEASURING PLASMA RENIN ACTIVITY: RESULTS IN HYPERTENSIVE PATIENTS.

Hiramatsu K, Yamada T, Yukimura Y, Komiya I, Ichikawa K, Ishihara M, Nagata H, Izumiyama T

(c/o Yamada) Dept. Medicine, Inst. Adaptation Medicine, Sch. Medicine, Shinshu Univ., Matsumoto, Japan

Arch Intern Med; 141(12):1589-1593 1981

In an attempt to devise a screening test for aldosterone-producing adenoma (APA) among hypertensive patients, the serum sodium and potassium levels, plasma renin activity (PRA), plasma aldosterone concentration, and aldosterone-PRA ratio were measured in 348 patients with hypertension. Nine patients with a substantially elevated aldosterone-PRA ratio were selected and hospitalized for further investigations. All nine patients were then recognized by scintigraphy with labeled cholesterol, venography, and surgical excision as having APA. The serum concentration of potassium was subnormal in three of nine patients with APA. In patients with APA, administration of diuretics and salt restriction significantly elevated PRA. However, even under notable diurnal and day-to-day variations of plasma aldosterone concentrations, the aldosterone-PRA ratio was always elevated inappropriately (more than 400) in patients with APA. In contrast, after administration of diuretics, both the PRA and aldosterone levels increased significantly in patients with essential hypertension, but the aldosterone-PRA ratio was less than 200. Since the renin-angiotensin system seems to be a major factor controlling aldosterone secretion in normal subjects, it is suggested that an elevation of aldosterone-PRA ratio more than 400 is a useful screening tool for the prediction of APA among hypertensive patients. (Author abstract) (25 Refs)

PANCREAS TUMORS

33. COMPUTED TOMOGRAPHY IN EVALUATION OF THE PANCREAS.

Weyman PJ, Stanley RJ, Levitt RG

Mallinckrodt Inst. Radiology, 510 South Kingshighway Blvd., St. Louis, MO, 63110

Semin Roentgenol; 16(4):301-311 1981

Computed tomography (CT) of the pancreas is reviewed and illustrated. Topics presented include technique, normal anatomy, pathologic changes (inflammatory lesions, neoplastic lesions: pancreatic tumors), and CT and other imaging methods. In 216 patients with pancreatic disease examined with a 3 sec EMI 7070 scanner, only 2 CTs were unsuccessful. Neoplasms discussed include pancreatic carcinoma, islet cell tumors, neoplasms involving the pancreas secondarily (lymphoma or metastases to peripancreatic lymph nodes), cystadenoma, and cystadenocarcinoma. Diagnosis by CT is examined with respect to ultrasound, endoscopic retrograde cholangiopancreatography, percutaneous needle biopsy, fine needle percutaneous transhepatic cholangiography, and pancreatic arteriography. (38 Refs)

34. HCG AND HCG SUBUNITS AS TUMOUR MARKERS IN PATIENTS WITH ENDOCRINE PANCREATIC TUMOURS AND CARCINOIDS.

Oberg K, Wide L
Dept. Internal Medicine, Univ. Hosp., Uppsala, Sweden
Acta Endocrinol (Copenh); 98(2):256-260 1981

Serum levels of hCG, hCG-alpha- and hCG-beta-subunits were measured in 29 patients with APUD-tumors, 16 patients with endocrine pancreatic tumors (EPT) and 13 patients with carcinoids. Twenty out of 29 patients (69%) had elevated level of hCG and its subunits. Among patients with EPT, 11 out of 16 (69%) had raised levels of these peptides. Three patients with benign tumors had normal concentrations, thus giving a frequency of 85% in the group of malignant EPT. In patients with carcinoids 9 out of 13 (69%) had elevated serum levels of at least one of the components. A discordance in secretion pattern between the two types of APUD-tumors was noticed. Only one patient, a case with a carcinoid had raised levels of the complete hCG molecule. The levels of hCG-alpha were elevated in 23% of the patients with malignant EPT and 69% of the patients with carcinoids while the corresponding frequencies of raised hCG-beta levels were 69% and 8%, respectively. Three out of four patients with so-called non-functioning islet cell tumors had raised levels of the subunits. These results indicate that hCG subunits are valuable tumor markers in both of these APUD-tumors, and that malignant EPT predominantly secrete hCG-beta- and carcinoids hCG-alpha-subunits. (Author abstract) (10 Refs)

GONADAL TUMORS

35. STEROID SECRETION AND TESTOSTERONE BINDING IN A WOMAN WITH AN OVARIAN HILUS CELL TUMOR AND THYROTOXICOSIS.

Sutton GP, Lyles KW, Wiebe RH
(c/o Wiebe) Dept. Obstetrics and Gynecology, Duke Univ. Medical Center, Duham, NC, 27710
Am J Obstet Gynecol; 141(5):535-538 1981

Presented is the case of a 21-yr-old woman with an ovarian hilus cell tumor and thyrotoxicosis. Despite massively elevated levels of serum testosterone, virilization was lacking and cyclic ovulatory menses were maintained. Hypersecretion of thyroxine and an increased circulating testosterone-estradiol globulin (TeBG) resulted in a level of free testosterone lower than expected, thereby perhaps accounting for the negligible androgen effect. Determinations of peripheral and ovarian venous steroids provided the first in vivo evidence for the preferred synthesis of testosterone via the delta5 pathway in a hilus cell tumor. (Author abstract) (13 Refs)

36. INCIDENCE OF HCG SUBUNITS IN PATIENTS WITH HCG-POSITIVE NONSEMINOMATOUS TESTICULAR GERM CELL TUMORS (MEETING ABSTRACT).

Mann K, Haidl P, Hammerl B, Karl HJ
Universitat Munchen, Munich, W. Germany
Acta Endocrinol [Suppl]; 96(240):80 1981

Human chorionic gonadotropin (HCG) determinations in serum are widely accepted to be useful as tumor markers in testicular cancer. Most anti-hCG-beta antisera available are sufficiently specific with respect to their cross-reactivity with pituitary hormones, but the interference of hCG subunits in heterologous hCG-beta radioimmunoassays is poorly explored. In order to evaluate the incidence of hCG subunits in sera with elevated hCG levels hCG, hCG-beta, and hCG-alpha were determined simultaneously using specific assays, 125I-hCG, anti-hCG-beta Serono, 125I-hCG-beta, anti-hCG-beta Union Carbide and 125I-hCG-alpha, anti-hCG-alpha 'Irmi'. Data of subunit determinations were corrected respecting the 2.2% cross-reactivity of hCG in the homologous hCG-beta assay and 6.4% in the alpha-assay. HCG and hCG-alpha levels were compared in 40 patients with nonseminomatous germ cells tumors. hCG, hCG-beta, and hCG-alpha in 25. The control group consisted of male patients without neoplastic, chronic inflammatory, thyroid or renal diseases. Labeled hCG, hCG-beta and hCG-alpha donated from NIAMD, was cochromatographed as an internal standard. Blue dextran, 125I and labeled hormones were also gel filtered in separate experiments for calibration. Five (20%) out of 25 hCG positive patients showed elevated hCG-beta levels and of 40 patients 4 (10%) had elevated hCG-alpha levels. Definite proof of subunit secretion was performed in 3 cases by gel chromatography of the patients' sera. In one patient immunoreactive hCG-beta showed two peaks, corresponding to 125I-hCG-beta and a high molecular from. HCG-alpha eluted in an identical position with 125I-hCG-alpha. These data demonstrate that hCG subunit secretion in patients with elevated hCG levels is not a negligible rare event and support our proposal that, for routine purposes, a hCG assay is preferable, which makes it possible to determine hCG and hCG-beta simultaneously on parallel standard curves, standardized with the 2nd International Reference Preparation of hCG. (no Refs)

37. LACTIC DEHYDROGENASE IN THE MONITORING AND PROGNOSIS OF TESTICULAR CANCER.

Lippert MC, Javadpour N
(c/o Javadpour), NCI, NIH, Room 10N222, Bethesda, MD, 20205
Cancer; 48(10):2274-2278 1981

In a prospective study of 80 patients with germinal testicular cancer, serial determinations of lactic dehydrogenase (LDH), alpha-fetoprotein (AFP) and human chorionic gonadotrophin (HCG) were followed for a mean of 18.1 mo. Serum LDH was found to be elevated more frequently with increasing tumor bulk. LDH was elevated in 78.0% of the patients with Stage III disease but only 26.3% of the Stage II patients and 20.0% of the pre-orchiectomy Stage I patients. In this study, serum HCG and AFP levels were always elevated in the presence of elevated serum LDH levels except in one patient when LDH was the only elevated marker, in which case it correlated with clinical disease. Correlation of these three serum markers is shown by elevation of LDH in 78.0% of the Stage III patients, AFP in 78.6%, and HCG in 76.2%. In addition, of the 43 patients who had normal LDH levels on initial presentation, their mean survival time (MST) at the end of the study was 15.5 mo while the 26 patients who had elevated LDH levels on initial presentation had an MST of 9.2 mo. Serum LDH, therefore, may be useful in evaluating patient prognosis as well as an adjunct in monitoring the treatment of patients with bulky testicular cancer. The combination of LDH and HCG has been utilized to monitor the treatment of seminoma. (Author abstract) (16 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

38. ESTROGEN AND PROGESTERONE RECEPTORS IN HUMAN BREAST CANCER: FREQUENCY AND DISTRIBUTION (MEETING ABSTRACT).

Zachariah NY, Chakmakjian ZH
Section of Endocrinology and Metabolism, Baylor University Medical Center, Dallas, TX, 75246
Clin Chem; 27(6):1077 1981

Determination of estrogen receptor (ER) and progesterone receptor (PR) has been useful in selecting patients for endocrine therapy. Using the conventional methods of determination, we have analyzed over 500 breast tumors for ER and PR; and classified them as positive (greater than 10fm/mg) negative (less than 3fm/mg) and borderline positive (4-9fm/mg). Fifty-two % of tumors were ER positive. However, 36% of the tumors were positive for both ER and PR. In order to establish the relationship between ER and PR in individual tumors, the quantitative correlation was studied in ER and PR positive tumors. It was found that 66.6% of the tumors were PR positive when ER was in the range of 10-40fm/mg; 78.2% PR positive when ER was 41-60fm/mg; and 85% PR positive when ER was 81-100fm/mg. Influence of menopausal status on the distribution of receptors indicate that 53.4% of post-menopausal women were ER positive while only 34.8% pre-menopausal women were ER positive. The ER content was also found to be higher in pre-menopausal women. (ER in post-menopausal 55.8fm/mg, while in pre-menopausal 29.3fm/mg). Menopausal status did not have a significant influence on PR distribution or the content. Also, quantitative relationship between ER and PR with respect to menopausal status indicates that a strong correlation exists in pre-menopausal patients. Similar correlation was not possible in post-menopausal patients. This study shows that: (a) definite influence of menopausal status on ER; its distribution and content (b) greater the ER content, more the chance for tumor to be PR positive (c) frequency of ER and PR positive tumors correlate with the reported clinical response. (no Refs)

39. ANDROGEN-INDUCED REMISSIONS AFTER ANTIESTROGEN AND HYPOPHYSECTOMY IN STAGE IV BREAST CANCER.

Manni A, Arafah BM, Pearson OH
Univ. Hosp. Cleveland, 2074 Abington Rd., Cleveland, OH, 44106
Cancer; 48(11):2507-2509 1981

Fluoxymesterone (Halotestin), 10 mg po BID, was given to 33 women with Stage IV breast cancer who had previously been treated with the antiestrogen tamoxifen (Nolvadex) and of whom 17 had also undergone hypophysectomy. Objective remissions were obtained in 13 patients (39%) with an av duration of 11+ mo. Response rate to fluoxymesterone was similar in patients who had previously responsed to tamoxifen and in those who had failed. Duration of response was longer in the former group (12+ vs 8 mo), but this difference was not statistically significant. Of 17 patients who had been previously treated with tamoxifen and hypophysectomy, 7 obtained further remission from fluoxymesterone for an av duration of 10 mo. Two patients with remissions from fluoxymesterone had previously failed to respond both to antiestrogen therapy and to the removal of the pituitary gland. Androgens appear to be an effective sequential endocrine treatment of Stage IV breast cancer after tamoxifen and hypophysectomy. The mechanism by which androgens induce tumor regression in some patients is probably not an antiestrogenic effect or an indirect effect mediated through the pituitary gland, but perhaps a direct action at the tumor level. (Author abstract) (11 Refs)

40. TAMOXIFEN IN BREAST CANCEROLOGY.

Bastit P
C.A.C. Henri-Becquerel, rue d'Amiens, 76038 Rouen Cedex, France
Gaz Med Fr; 88(30):4207-4208 1981

The use of tamoxifen (TX), an agent which selectively inhibits the action of estrogen on certain tissues, particularly the breast, in breast cancer therapy is discussed. TX (1-3 tablets, 10 mg/day) is used in the treatment of locoregional breast tumors. The rate of lesion regression (complete or greater than 50%) following TX treatment is approx 30%. TX is more effective against soft tissue involvement as compared with bony metastases. Some wk are often required for the appearance of TX therapeutic effects. TX is most effective when used in previously untreated patients and in those greater than 60 yr of age. Postmenopausal patients show a better response to TX than do premenopausal patients. Patient tolerance to TX treatment is generally good. Nausea and vomiting resulting from TX treatment is usually moderate, disappearing after several days or wk of treatment; flushing and amenorrhea may also result. Biologically TX causes a decrease in WBC and platelets. Hypercalcemia and liver disorders may also be observed. (no Refs) (In FRE)

41. TOPICAL ASPECTS OF HORMONE THERAPY FOR PROSTATE CARCINOMA.

Altwein JE
Urologische Abteilung, Bundeswehr Krankenhaus, Oberer Eselsberg 40, D-7900 Ulm, W. Germany
Helv Chir Acta; 48(3/4):391-395 1981

Four endocrine treatment modalities for prostate carcinoma were analyzed in a Phase III study including randomization and classification by prognostic parameters: 1. Primary orchiectomy with hormones only after tumor progression; 2. Primary estrogens with orchiectomy only after tumor progression; 3. Primary treatment with cyproterone acetate (CA) or medroxyprogesterone acetate; 4. Combined hormone therapy [estramustine phosphate (EP), cyproterone acetate, or estrogens plus bromocriptine]. CA was no more or less cancerostatic than estrogen, but its side effects were fewer. Estrogens and CA caused a rise in serum prolactin that justified use of the antiprolactin agent bromocriptine. Simultaneous orchiectomy provided no advantage, except in cases of urine retention. Late orchiectomy could be used if other measures failed to stop tumor progression. EP was recommended only in cases of relapse. (14 Refs) (In GER)

42. RADIOIMMUNOASSAY OF TISSUE STEROIDS IN ADENOCARCINOMA OF THE PROSTATE.

Belis JA, Tarry WF
Dept. Urology, West Virginia Univ., Morgantown, WV, 26506
Cancer; 48(11):2416-2419 1981

Tissue steroid levels in 48 needle-biopsy samples of adenocarcinoma of the prostate were quantified by radioimmunoassay (RIA). Tissue levels of dihydrotestosterone (DHT), estradiol-17beta, and estrone were correlated with tumor stage, histologic grade, and patient response to endocrine therapy. All patients with well-differentiated carcinoma of the prostate had tissue DHT content greater than 2.0 ng/g while 35% of patients with moderately differentiated or poorly differentiated tumors had tissue DHT content less than 2.0 ng/g. DHT content appeared to be unrelated to tumor stage. Estradiol and estrone content correlated well with tumor grade but not with tumor stage. DHT levels were measured in 17 patients with symptomatic Stage D2 carcinoma of the prostate. Thirteen patients with DHT content greater than 2.0 ng/g initially had an objective and/or subjective response to endocrine therapy. Four patients with tissue DHT levels below 2.0 ng/g had no response to hormonal therapy. Quantification of tissue DHT content by RIA is a promising method for predicting initial response to hormonal therapy in adenocarcinoma of the prostate. (Author abstract) (16 Refs)

43. SOMATOSTATIN-LIKE IMMUNOREACTIVITY IN MID-GUT CARCINOIDS.

Lundqvist M, Wilander E
Dept. Pathology, Univ. Uppsala, S-751 22, Uppsala, Sweden
Acta Pathol Microbiol Scand [A]; 89(4):335-337 1981

Typical mid-gut carcinoids from 18 patients without endocrine syndromes were examined for the presence of somatostatin-immunoreactive tumor cells. Positively stained cells were found in six tumors (33%), but they did not constitute the majority cell population in any of the cases. The results further emphasize the multihormonal nature of mid-gut carcinoid tumors. (Author abstract) (10 Refs)

44. IMMUNOHISTOCHEMICAL EVIDENCE OF PEPTIDE HORMONES IN ENDOCRINE TUMORS OF THE RECTUM.

Alumets J, Alm P, Falkmer S, Hakanson R, Ljungberg O, Martensson H, Sundler F, Tibblin S
Dept. Histology, Univ. Lund, Biskopsgatan 5, S-223 62 Lund, Sweden
Cancer; 48(11):2409-2415 1981

Twenty-five endocrine tumors of the rectum (rectal carcinoids) were examined immunohistochemically for various pancreatic and gut neurohormonal polypeptides. Twenty-one of the tumors were found to contain cells displaying pancreatic polypeptide (PP), glucagon, somatostatin, insulin, substance P, enkephalin or beta-endorphin immunoreactivity. At least 11 of the tumors contained more than one peptide hormone. In some of the tumors PP cells made up the major cell population, in others the glucagon cells constituted the majority. Only four of the tumors contained 5-hydroxytryptamine. Rectal endocrine tumors seem unique among gut endocrine tumors in that they may store immunoreactive enkephalin, beta-endorphin and even insulin. None of the patients displayed the carcinoid syndrome; symptoms were usually vague and uncharacteristic. In many cases the tumor was found at routine examination. (Author abstract) (37 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

45. PSEUDO-ZOLLINGER-ELLISON SYNDROME. HYPERGASTRINEMIA, HYPERCHLORHYDRIA WITHOUT TUMOR.

Friesen SR, Tomita T
Dept. Surgery, Univ. Kansas Medical Center and Coll. Health Sciences, Kansas City, KS, 66103
Ann Surg; 194(4):481-493 1981

The purpose of the investigation was to detect ulcer patients having nontumorous hypergastrinemic hyperchlorhydria and to diagnostically differentiate this pseudo-Zollinger-Ellison syndrome from neurogenic duodenal ulcer disease and pancreatic gastrinomas. Nine patients having clinical, radiologic and humoral findings simulating the Zollinger-Ellison syndrome or severe duodenal ulcer disease were studied by physiologic provocative testing. The patients, not having pancreaticoduodenal gastrinomas, had an antral mucosal source of their moderate hypergastrinemia even after vagotomy with drainage, which was eliminated in eight patients treated by surgical antrectomy, resulting in normal serum gastrin concentrations. The pseudo-Zollinger-Ellison syndrome is, thus, characterized physiologically by an exaggerated gastrin response to meals, no response to secretin stimulation and pathologically by hyperfunctioning hyperplastic G cells of the antrum. The clinical, physiologic, pathologic, and surgical features were integrated for accurate diagnosis and treatment. (Author abstract) (46 Refs)

46. BONE RESORPTION AND HUMORAL HYPERCALCEMIA OF MALIGNANCY: STIMULATION OF BONE RESORPTION IN VITRO BY TUMOR EXTRACTS IS INHIBITED BY PROSTAGLANDIN SYNTHESIS INHIBITORS.

Minkin C, Fredericks RS, Pokress S, Rude RK, Sharp CF, Tong M, Singer FR
Dept. Basic Sciences - Physiology Section, Univ. Southern California Sch. Dentistry, Post Office Box 77951, Los Angeles, CA, 90007
J Clin Endocrinol Metab; 53(5):941-947 1981

Extracts of tumors from patients with humoral hypercalcemia of malignancy (HHM) were tested using an in vitro bone resorption assay in order to investigate the pathogenesis of the hypercalcemia. Bone resorption was assessed by comparing the percent release of previously incorporated 45Ca from paired halves of newborn mouse calvaria. Saline extracts of three out of five tumors from HHM patients caused a significant increase in 45Ca release relative to controls. Extracts of liver and non-HHM tumor did not cause significant resorption. Tumor-stimulated bone resorption was blocked by indomethacin and eicosatetraynoic acid, inhibitors of the synthesis of prostaglandins (PGs) and related metabolites of arachidonic acid, whereas resorption stimulated by parathyroid hormone (PTH), PGE2, or 1,25-(OH)2D3 was not. Furthermore, levels of immunoreactive PTH or PGE2 in tumor extracts were not sufficient to account for the degree of resorption observed. These observations indicate that PTH or PGE2 are not responsible for the bone resorption caused by extracts of tumors from these patients with HHM. Furthermore, they suggest that hypercalcemia in these patients may result from bone resorption stimulated by the local production in bone of PGs or related metabolites of arachidonic acid in response to a humoral factor elaborated by the tumor. (Author abstract) (28 Refs)

47. MALIGNANCY-ASSOCIATED HYPERCALCEMIA: EVALUATION WITH A CYTOCHEMICAL BIOASSAY FOR PARATHYROID HORMONE.

Goltzman D, Stewart AF, Broadus AE
Dept. Medicine, Royal Victoria Hosp., Montreal H3A 1A1, Canada
J Clin Endocrinol Metab; 53(5):899-904 1981

Employing a cytochemical assay initially developed for measuring parathyroid hormone (PTH), bioactivity was assessed in 33 patients with malignancies. Initial studies in vitro were consistent with a role for cAMP as a second messenger in the bioassay. Cytochemical bioactivity was increased in the peripheral plasma of 10 of 16 hypercalcemic patients with elevated nephrogenous cAMP excretion, and mean levels were 10-fold higher in these patients than in 17 normocalcemic or hypercalcemic patients with normal or suppressed nephrogenous cAMP excretion, respectively. Plasma bioactivity, serum calcium, and nephrogenous cAMP excretion all fell to normal in one patient after tumor resection, and cytochemical bioactivity was demonstrable in the tissue culture medium in which the neoplasm was maintained. Gel chromatographic analysis revealed that a major component of plasma bioactivity eluted before rather than with PTH-(1-84) in patients with malignancy in contrast with that in patients with primary hyperparathyroidism. The studies, therefore, demonstrate the capacity of the cytochemical bioassay to measure increased activity in patients with malignancy, hypercalcemia, and elevated nephrogenous cAMP excretion; suggest that the material responsible for the activity differs from PTH-(1-84); and provide a sensitive detector system for further analysis of this material and its role in the pathogenesis of this disease. (Author abstract) (22 Refs)

48. HYPOTHYROIDISM FOLLOWING TREATMENT FOR HEAD AND NECK CANCER.

Vrabec DP, Heffron TJ
Dept. Otolaryngology, Geisinger Medical Center, Danville, PA, 17822
Ann Otol Rhinol Laryngol; 90(5,part1):449-453 1981

One hundred ninety-six head and neck patients were studied to determine the effects of radiation therapy and surgery on thyroid function. Serum thyroid-stimulating hormone (TSH) levels were obtained as a screening test for primary hypothyroidism. Elevated TSH levels were found in 57 of the 196 patients (29.1%). The highest incidence of abnormal TSH values (66%) occurred in the group treated with combination radiation therapy and surgery, including partial thyroidectomy. TSH levels rose early in the posttreat ment period with 60% of the abnormal values occurring within the first 3 posttreatment yr. Posttreatment thyroid dysfunction was twice as common in women (48.6%) as in men (25.4). When serum thyroxine levels by radioimmunoassay (T4RIA) were correlated with the elevated serum TSH levels, a similar pattern was seen with 65% of the patients in Group 3 having a decreased T4RIA level indicating overt hypothyroidism. Pretreatment levels of thyroid function including thyroid antibody studies should be established for all patients. Serial TSH levels should be done every 3 mo during the first 3 posttreatment yr and semiannually thereafter as long as the patient will return for follow-up care. All patients treated with combination radiation therapy and surgery who develop elevated TSH levels should be treated with thyroid replacement therapy. Patients receiving radiation therapy alone should receive replacement thyroid therapy if they develop a depressed T4RIA value or a pattern of gradually increasing TSH levels. (Author abstract) (19 Refs)

49. HYPOPARATHYROIDISM AND HYPOCALCAEMIA DURING THERAPY FOR ACUTE LEUKEMIA (MEETING ABSTRACT).

Freeman DB, Shannon MS, Prentice HG, Dandona P
Department of Haematology and Metabolic Unit, Royal Free Hospital, Pond Street, London NW3 2QG, England
Clin Sci; 61(3):25P 1981

We have recently observed that very low plasma concentrations of calcium and magnesium often occur in patients with acute leukemia during their treatment. These metabolic abnormalities present considerable diagnostic and management problems. We decided to investigate these phenomena. Eight patients with acute leukemia (acute myeloid 3; acute lymphoblastic 5) developed significant hypocalcemia (plasma calcium range 1.39-2.0 mmol/l) during treatment for their condition. These patients were normocalcemic prior to therapy. Three of the patients developed tetany or other overt hypocalcemic symptoms. Four of the patients who had lowest plasma calcium also concurrently had hypomagnesemia (range 0.28-0.65 mmol/l), and 2 had hyperphosphatemia; other patients' serum magnesium was at the lower end of the normal range (0.70 mmol/l). Immunoreactive parathyroid hormone (IRT) was undetectable in the sera of 3 patients, 2 of who had the lowest calcium concentrations and elevated phosphate levels; it was within the normal reference values (52-120 ng/ml) in 4 and only midly elevated in 1 (150 ng/ml despite plasma calcium concentrations of 1.75 mmol/l). Thus in all patients studied the serum parathyroid hormone concentration was either low in absolute terms or inappropriately low for the prevalent calcium concentration. These patients, therefore, had a state of absolute or relative hypoarathyroidism. (no Refs)

50. HYPERTHYROIDISM IN GESTATIONAL TROPHOBLASTIC NEOPLASIA.

Norman RJ, Green-Thompson RW, Jialal I, Soutter WP, Pillay NL, Joubert SM
Dept. Chemical Pathology, Univ. Natal, Post Office Box 17039, Congella 4013, Durban, South Africa
Clin Endocrinol (Oxf); 15(4):395-401 1981

The thyroid status of 27 African patients with gestational trophoblastic neoplasia (GTN) was studied. Fifteen patients were found to be biochemically hyperthyroid (8 patients with choriocarcinoma; 7 with hydatidiform mole). Of these 15 patients, 9 were clinically thyrotoxic. The most serious complication of thyrotoxicosis was life-threatening acute pulmonary edema with associated cardiac failure. It was found that when serum levels of the human chorionic gonadotrophin (hCG) reached a level of about 0.1 x 10(6) iu/l, 13 of 16 patients were biochemically hyperthyroid; at serum levels of 0.3 x 10(6) iu/l of hCG most patients were clinically thyrotoxic. A feature of hyperthyroidism associated with GTN is that whereas T4 is invariably raised the T3:T4 ratio tends to be low (0.015 +-005); rT3:T3 ratios were high in this group. TSH levels were not increased. (Author abstract) (15 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

51. RECOGNIZING HYPERPARATHYROIDISM CAUSED BY ECTOPIC PRODUCTION OF A SUBSTANCE RESEMBLING PARATHYROID HORMONE.

Ernst P, Kaye M
Montreal General Hosp., 1650 Cedar Ave., Montreal, PQ H3G 1A4, Canada
Can Med Assoc J; 125(8):857-859 1981

Criteria for differentiating hyperparathyroidism due to parathyroid adenoma from that due to ectopic secretion of a tumor is presented by way of an illustrative case study. The study involved a 75 yr old man suffering from hypercalcemia secondary to an occult squamous cell carcinoma of the lung. Symptoms included a decrease in well being, anorexia, weakness, 4.5 kg wt loss, chronic cough, increase in the serum concentration of calcium (3.5 milliM mM/l), and creatinine(150uM/l), and decrease in the serum concentration of phosphorus (0.7 mM/l). Urine levels of calcium, cyclic adenosine 3'5'monophosphate(cyclic AMP) and tubular reabsorption were decreased (10.9 mM, 1.7 uM/g creatinine, and 53%, respectively). Measurement of parathyroid hormone(PTH) levels were inconsistent. Other investigative procedures, including chest roentgenography and bone biopsies were interpreted as normal. Focal seizures led to discovery of two brain metastases; a review of the chest roentgenograms and tomography of the mediastinum led to the diagnosis of squamous cell carcinoma of the lung. Distinguishing features of pseudohyperparathyroidism include, most importantly, a short (2-6 mo) history, pronounced wt loss (often greater than 10 kg), renal calculi in less than 10% of cases, absence of pancreatitis and peptic ulcers, and serum calcium levels greater than 3.5 mM/l. Helpful specialized studies include serum concentration of immunoreactive PTH(increased levels suggest primary hyperparathyroidism) and urinary excretion of cyclic AMP(low values suggest pseudohyperparathyroidism). Hypercalcemia is a common clinical problem with diagnosis usually resting between hyperparathyroidism and pseudohyperparathyroidism. (15 Refs)

52. ECTOPIC HORMONE PRODUCTION BY ENDOCRINE TUMORS: LOCALIZATION OF HORMONES AT THE CELLULAR LEVEL BY IMMUNOCYTOCHEMISTRY.

Heitz PU, Kloppel G, Polak JM, Staub JJ
Dept. Pathology, Univ. Basel, Schonbeinstrasse 40, CH-4056 Basel, Switzerland
Cancer; 48(9):2029-2037 1981

Clinical and laboratory data, histologic, electron microscopic and immunocytochemical findings of the tumors of eight patients suffering from Cushing's syndrome and of one patient with hypercalcemia are described. The unlabeled antibody enzyme method was used for the detection of insulin, glucagon, somatostatin, pancreatic polypeptide, corticotropin, beta-lipotropin, calcitonin, parathyroid hormone, and gastrin. Ectopic Cushing's syndrome was caused by pancreatic endocrine tumors, medullary thyroid carcinoma, a bronchial a gastric and a thymic carcinoid, and a carcinoid of the mediastinum. Hypercalcemia in one patient was related to a pancreatic endocrine tumor. After surgery the clinical symptoms disappeared in two patients, but persisted or relapsed in five patients. ACTH-immunoreactivity could be demonstrated in six of eight tumors; calcitonin-immunoreactivity was found in the tumor of the patient suffering from hypercalcemia. ACTH-immunoreactivity could be localized to secretory granules by immunoelectron microscopy, and the presence of ACTH and beta-LPH in the same tumor cells could be shown in one pancreatic tumor. A combination of production of orthotopic and ectopic hormones was found in one, and secretion of two ectopic hormones was detected in another pancreatic endocrine tumor. (Author abstract) (41 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

53. BROMOCRIPTINE-INDUCED CHANGES IN HORMONE SECRETION AND CELL MORPHOLOGY IN GROWTH HORMONE AND PROLACTIN PRODUCING PITUITARY ADENOMAS.

Anniko M, Werner S, Wersall J
Dept. Oto-Rhino-Laryngology, Karolinska Sjukhuset, S-104 01 Stockholm, Sweden
Acta Otolaryngol (Stockh); 92(3/4):343-355 1981

Of two patients with GH-producing adenomas and two patients with prolactinomas treated with bromocriptine prior to operation, morphological changes in a limited number of pituitary tumor cells were observed only in two cases of PRL-secreting adenomas. The two patients with hypersecretion of GH did not show morphological damage of the pituitary tumor cells. In vitro incubation of post-pregnancy hyperplastic pituitary tissue with 0.1 and 0.001 ug/ml of bromocriptine did not affect hormone secretion or cell morphology. Tissue cultured in vitro from the prolactinomas exposed to bromocriptine in vivo prior to operation was affected with regard to both hormone secretion and cell morphology when exposing organ cultures to 0.1 and 0.01 ug/ml of bromocriptine. However, considerable variations in morphological damage occurred between the various parts of the tumor. GH secretion in prolactinomas was not affected by bromocriptine. In organ cultures of tumors with concomitant over-secretion of GH and PRL, an inhibition of the synthesis/secretion of PRL occurred without morphological evidence of cell damage when using concentrations of 0.1 and 0.01 ug/ml of bromocriptine. Ultrastructurally an increased number of lysosomes was indicated in exposed organ cultures. In tumors primarily secreting GH, incubation of organ cultures with bromocriptine caused individual variations of hormone secretion among the tumors. In one, the concentration of 0.1-1.0 ug/ml of bromocriptine caused a decrease of the PRL levels in the culture media, whereas in other tumors these concentrations did not affect PRL levels. The secretion of GH into the culture medium was not affected by bromocriptine in concentrations 0.001-1.0 ug/ml during incubation for 4-20 days. Pituitary tumor cells in vivo exposed to bromocriptine frequently showed extensively pleomorphic secretory granules. This ultrastructural abnormality disappeared when culturing specimens in the in vitro system. (Author abstract) (29 Refs)

54. RELATIONSHIP BETWEEN BIOLOGICAL RESPONSIVENESS TO PHORBOL ESTERS AND RECEPTOR LEVELS IN GH4C1 RAT PITUITARY CELLS.

Jaken S, Tashijian AH, Blumberg PM
(c/o Blumberg) Dept. Pharmacology, Harvard Medical Sch., Boston, MA, 02115
Cancer Res; 41(12):4956-4960 1981

During a 24-hr incubation of GH4C1 cells with phorbol esters or thyrotropin-releasing hormone, there is a decrease in the number of phorbol ester receptors (down-modulation). The purpose of this study was to investigate whether this decrease in receptor number attenuated cellular responsiveness to subsequent challenge with phorbol esters. Accordingly, cellular sensitivity to a phorbol ester-mediated biological response, namely the decrease in binding of epidermal growth factor, was compared in control and down-modulated cells. This phorbol ester-mediated event is closely associated with phorbol ester receptor occupancy, and it is therefore an effect for which altered dose-response characteristics correlating with alterations in the number of phorbol ester receptors could be anticipated. In fact, during a 48-hr exposure to phorbol esters, GH4C1 cells become refractory to the effect on epidermal growth factor binding. This time course is similar to that for the loss of phorbol ester receptors. However, when cells are down modulated by pretreatment with phorbol ester or thyrotropin-releasing hormone and then (re)challenged with phorbol ester, no differences in dose-response characteristics were observed between control an d down-modulated cells. We therefore conclude that phorbol ester receptor down-modulation does not affect cellular responsiveness to phorbol esters, at least when decreased epidermal growth factor binding is used as the marker for the phorbol ester-mediated event. (Author abstract) (21 Refs)

55. SPONTANEOUS TUMORS IN THE ADRENAL MEDULLA OF LONG-EVANS RATS (MEETING ABSTRACT).

Wilson-Martino NA, McCarthy KJ, Mankes RF, Benitz KF
Institute of Experimental Pathology and Toxicology, The Albany Medical, College Albany, NY, 12208
Toxicologist; 1(1):153 1981

On the basis of reported longevity and low incidence of spontaneous neoplastic processes, 360 Long-Evans rats from Blue Spruce Farms were fed the organophosphate pesticide NTN 8629 at dietary concentrations of 0.5 and 25ppm for 2 yr. Although no adverse affects, directly attributable to the administration of NTN 8629, were elicited, the incidence of 16.4% (or 57/348) of neoplastic processes in the adrenal medulla was far greater than expected in this strain of rats. Of these 57 cases, 38 were selected for detailed pathologic characterization (on the basis of technical considerations) and evaluated for: wt, laterality, local invasiveness, vascular erosion, peripheral dissemination (tumor emboli), metastases, alveolar pattern, papillary pattern, vasculature, analplasticity, mitotic activity and peripheral compression. Of the 38 tumors, 30 were benign pheochromocytomas while 8 pheochromoblastomas showed signs of malignancy with local invasiveness, vascular erosion, intra-vascular, tumor emboli, local and distant metastases. Only 1 malignant neoplasm was found in a female. The remaining 7 were all in males. The most malignant case was found in a male control with local spread and distant metastases to the lungs and both kidneys. Of the 30 benign tumors, 15 were found in males and an equal number in females. (no Refs)

56. INHIBITION OF PROSTATE TUMOR GROWTH IN TWO RAT MODELS BY CHRONIC ADMINISTRATION OF D-TRP6 ANALOGUE OF LUTEINIZING HORMONE-RELEASING HORMONE.

Redding TW, Schally AV
Endocrine and Polypeptide Lab., Veterans Admin. Medical Center, New Orleans, LA, 70146
Proc Natl Acad Sci USA; 78(10):6509-6512 1981

We have investigated the effect of the D-Trp6 analogue of luteinizing hormone-releasing hormone (LH-RH), a superactive analogue of LH-RH, on the growth of two different models of prostate tumors in rats. Chronic administration of D-Trp(6)-LH-RH in a dose of 25 ug/day for 14-21 days significantly inhibited the growth of the chemically induced squamous cell carcinoma 11095 in Fisher 344 male rats. The wt of the ventral prostate and testes were also significantly reduced by treatment with this analogue. After 21 days of treatment, the animals no longer showed increases in serum luteinizing hormone and follicle-sti mulating hormone levels in response to D-Trp(6)-LH-RH. Treatment of male Copenhagen F-1 rats bearing the Dunning 3327 prostate adenocarcinoma with 25 ug of D-Trp(6)-LH-RH per day for 42 days decreased the wt of both the ventral prostate and testes but had no effect on the wt of the anterior pituitary gland. The percentage increase in tumor vol was decreased to one-third and the actual tumor wt was decreased by 58% compared to untreated controls. The tumor doubling time was more than 4x longer in rats receiving D-Trp(6)-LH-RH than in controls. Serum levels of luteinizing hormone and follicle-stimulating hormone were significantly decreased in rats receiving this analogue. In both Fisher 344 and Copenhagen F-1 rats, serum prolactin and testosterone levels were significantly decreased after treatment with D-Trp(6)-LH-RH, whereas progesterone levels were increased. (Author abstract) (34 Refs)

57. CHARACTERIZATION OF CALCITONIN- AND ADRENOCORTICOTROPIN-PRODUCING HUMAN CLONED CELL LINES.

Dermody WC, Rosen MA, Ananthaswamy R, Levy AG, Hixson CV, Aldenderfer PH, Nelson-Rees WA, Marangos PJ, Swanson EC
American Dade, P.O. Box 520672, Miami, FL, 33152
J Clin Endocrinol Metab; 53(5):970-977 1981

We have developed three human cloned cell lines that produce immunoreactive human calcitonin (ihCT) and ACTH (iACTH) as well as exhibit characteristics of cultured neural cells. Clones HMS-41/I,-78/2, and-98/2 were developed from cell lines HeLa AV3, MBA 9812 (bronchogenic carcinoma), and SW 267 (pheochromocytoma), respectively. Karyological analysis of both the parent and the cloned cell lines confirmed the identity of HeLa AV3 and MBA 9812. When grown in serum-free media designed for culturing neural cells, the patterns of production for both ihCT and iACTH varied among the clones. The multiple patterns of hormone production suggest that the mechanisms involved in the biosynthesis, processing, and secretion of these hormones differ among the clones. The clones contain neuron-specific enolase and the putative neurotransmitters beta-alanine and gamma-amino butyric acid, and they respond to cAMP analogs by differentiating, as noted by the extension of neurites (except the HeLa-derived HMS-41/I). The iACTH extracted from cells and synthetic ACTH exhibited equivalent profiles upon isoelectric focusing. The forms of ihCT noted in cell extracts were similar to those observed in extracts of human tumor tissue. Our rabbit antiserum to hCT failed to detect ihCT in those cell extracts prepared for ACTH determination or in extracts of rat pituitaries, but it did detect CT in rat thyroids by both RIA and immunofluorescent procedures. We concluded that our antisera to hCT do not detect the precursor form of ACTH. The availability of these cloned cell lines provides model systems for examining the production of these peptide hormones and the concomitant expression of neura l and endocrine characteristics. (Author abstract) (56 Refs)

58. HYPERENINEMIC HYPOALDOSTERONISM IN ASSOCIATION WITH NEOPLASIA INDUCED HYPERCALCEMIA IN THE FISCHER RAT.

Sowers JR, Sollars E, Nyby MD, Jasberg K, Tuck ML
Endocrine Metabolism Div. (111E), Veterans Admin. Medical Center, 16111 Plummer St., Sepulveda, CA, 91343
Metabolism; 30(10):987-991 1981

Alterations in the renin-angiotensin-adolosterone system in hypertensive, hypercalcemic Fischer rats bearing transplanted Leydig cell tumors were evaluated by measuring plasma aldosterone (PA), plasma renin activity (PRA), and systolic blood pressure (BP) responses to immobilization stress. PA and plasma corticosterone responses to graded ATCH infusions and PA and BP responses to graded angiotensin II (AII) were also evaluated. The results demonstrated marked increases in basal PRA that correlated with the degree of hypercalcemia reached after tumor transplanation. Postive correlations between serum calcium and PRA suggested that increased calcium ion stimulated renin secretion. PRA responses to immobilization stress were increased in tumor-bearing rats. However, basal PA and corticosterone levels were decreased in hypercalcemic rats, as were PA and corticosterone responses to ACTH and PA responsess to immobilization stress and AII. BP responses to immobilization stress and AII correlated positively with serum calcium concentrations. The possibility that the hypertension in these rats was related to a vasoconstrictor effect of calcium on peripheral blood vessels is discussed. (28 Refs)

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Consulting reviewer:
NAGUIB A. SAMAAN, M.D., Ph.D.

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. RELATIVE VALUE OF COMPUTED TOMOGRAPHY AND HYPOCYCLOIDAL TOMOGRAPHY IN THE DIAGNOSIS OF PITUITARY MICROADENOMA: A RADIO-SURGICAL CORRELATIVE STUDY.

Bonafe A, Sobel D, Manelfe C
Dept. Neuroradiology, Centre Hospitalier Universitaire de Purpan, Toulouse Cedex, France
Neuroradiology; 22(3):133-137 1981

The relative value of a second generation CT scanner and complex motion polytomography are compared in 36 patients undergoing transsphenoidal surgery due to clinical and biologi-

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cal evidence of pituitary hypersecretion. CT findings of focal glandular hypodensity in 17 patients and upward convexity of the sellar contents in 15 patients suggested the presence of a pituitary microadenoma. Complex motion tomographic findings suggesting a microadenoma were found in 21 of 32 cases and included bulging of the sellar floor or localized thinning of the lamina dura. Selective transsphenoidal adenomectomy was performed on 34 of the 36 patients and the preoperative location based on CT scanning data was positively correlated with surgical results in 75% of the cases. When there is a strong clinical suspicion of pituitary hypersecretion both CT and polytomography may suggest the existence and location of a microadenoma. CT should be the radiographic technique of choice since it produces accurate information as to the size and density of the pituitary gland. (Author abstract) (27 Refs)

2. PATTERNS OF CORTICOTROPIC CELLS IN THE ADULT HUMAN PITUITARY IN CUSHING'S DISEASE.

McNicol AM
Univ. Dept Pathology, Royal Infirmary, Glasgow, Scotland
Diagn Histopathol; 4(4):335-341 1981

Pituitary glands from nine patients who died of Cushing's disease were studied. Staining with an immunoperoxidase technique revealed three patterns of corticotropic cells. Three pituitaries showed a pattern which could not be distinguished from normal. Three pituitaries contained an ACTH cell adenoma and a marked reduction in the total number of ACTH cells in the remainder of the gland; two of the tumors were microadenomas, but the whole tumor of the third adenoma was not available for assessment. In the third group, two of the pituitaries contained large aggregates of ACTH cells which by size and morphological appearance had been diagnosed as adenomas; the third pituitary showed hyperplasia of ACTH cells with nodules but without a large aggregate of ACTH cells. Two populations of corticotrophic cells may exist within the adult human pituitary; the populations appear to correspond to the anatomical distribution of anterior and intermediate lobe corticotrophs. (46 Refs)

3. SURGICAL TREATMENT OF PITUITARY ADENOMAS: EARLY OR LATE DIAGNOSIS AND TREATMENT.

Nesbakken R, Reinlie S, Norman N
Dept. Neurosurgery, Ulleval Hosp., Oslo, Norway
J Oslo City Hosp; 31(10):117-127 1981

Fifty patients with pituitary adenomas, who were diagnosed without the help of the ophthalmologist, were treated by transsphenoidal microsurgery according to the methods of Cushing, Guiot, and Hardy. All were evaluated by an endocrinologist and all had x-ray findings consistent with a pituitary lesion, and all but one had positive endocrinological findings. Immediate endocrine changes (prolactin [PRL], growth hormone, thyroid stimulating hormone) during and after tumor excision were followed by sequential blood sampling, with later samples analyzed by radioimmunoassay. There was one diagnostic failure, and one serious operative complication, purulent meningitis. Early hormone assays indicate radical surgery if serum PRL is less than 500 ug/liter (except in one patient in whom surgery was terminated because orientation was lost). (7 Refs)

4. SURGERY OF THE PITUITARY GLAND.

Tindall GT, Tindall SC
Dept. Neurosurgery, Emory Univ. Sch. Medicine, Atlant
Curr Probl Surg; 18(10):610-679 1981

Diagnostic and therapeutic advances in the mar
pituitary disorders and effects of these developm
treatment of endocrine-sensitive breast and prostate
reviewed. Specific topics covered include pitu
anatomy; incidence, pathology, and clinical featu
itary tumors; diagnostic endocrinologic and neu
studies; and treatment protocols for the following s
itary abnormalities: asymptomatic enlarged sella
empty sella syndrome, tumors causing mass effects
secreting adenomas, acromegaly, and Cushing's dise
son's syndrome. Steps in transsphenoidal and and
pituitary surgery, postoperative management, and
tions of surgery are discussed. Management of resi
current adenomas, recurrent or persistent hyp
tumors, and recurrent nonfunctional tumors is also
Indications for hypophysectomy in breast and pros
are discussed along with hypophysectomy technique
operative patient management. (162 Refs)

5. EFFECT OF CIMETIDINE ON SERUM PROLA NORMAL WOMEN AND PATIENTS WITH HYPERPROLACTINEMIA.

Carlson HE, Chang RJ, Meyer NV, Lu KH, Judd HL
Endocrinology Section, Veterans Administration Wadswo
Center, Wilshire and Sawtelle Boulevards, Los Angeles,
Clin Endocrinol (Oxf); 15(5):491-498 1981

The effects of cimetidine (CMT) on pituitary ho
lease were studied in eight normal women (22-41 y
20 patients (7 men, 13 women; 20-61 yr old) with no
al hyperprolactinemia (6 prolactinoma, 2 acromegaly
thalamic cysts, and 10 idiopathic hyperprolactinemia)
post-partum women were also studied as a model
logical hyperprolactinemia. Following iv CMT
serum prolactin (PRL) in normal women rose sig
from a mean baseline value of 7.7 +-2.3 nanog/ml to
33.7 +-4.5 nanog/ml (p less than 0.005). Serum gro
mone, thyrotrophin, luteinizing hormone, and follicle
ing hormone were not significantly altered after CMT
tration. Six of eight patients with pituitary tumors
lower PRL response to iv CMT than normal wome
tumor patients, the absolute PRL response to thyrotr
leasing hormone (TRH) was greater than the response
(p less than 0.05). In only 4/8 patients, did the absol
less than response to TRH fall below the range seen
women. When expressed as a percentage increment o
line, the PRL responses to both CMT and TRH were
ly blunted when compared to normal women, with n
between the tumor and normal groups. The percenta
ments in PRL were greater following TRH than CM
tumor subjects (p less than 0.05). Approx half of idiop
perprolactinemia patients showed lower PRL response
CMT and TRH than normal women; in 7/10 subjects
solute response to TRH was greater than the response
(p less than 0.05). The two patients with hypothalami
showed responses generally similar to those of the
two groups. Post-partum subjects tended to have e
PRL response to provocative tests. The results indica
dynamic testing of PRL secretion with CMT is no mo
than TRH in distinguishing tumorous from non-tumo
perprolactinemia. (24 Refs)

6. EFFECTS OF BROMOCRIPTINE-INDUCED PREGNANCY ON PROLACTIN-SECRETING PITUITARY TUMOURS.

Bergh T, Nillius SJ, Larsson SG, Wide L
Dept. Obstetrics, Univ. Hosp., Uppsala, Sweden
Acta Endocrinol (Copenh); 98(3):333-338 1981

Twenty-eight women with hyperprolactinemia and amenorrhea received bromocriptine treatment which resulted in 31 term pregnancies. Bromocriptine treatment was stopped as soon as pregnancy was established. Nineteen of the women had radiological signs of a pituitary tumor. The pregnancies were clinically uneventful in all cases except one who developed headache. Post-partum sellar x-ray showed pregnancy-induced enlargement of the pituitary fossa in 4 of the 28 women. Regression of the radiological changes occurred in three of the four women within 2 yr after the delivery. The women with abnormal sellar x-rays had no difference in the mean prolactin levels before treatment and after pregnancy and lactation while all the women with normal sellae had lower prolactin levels after pregnancy than before. Three women resumed regular spontaneous menstruations after pregnancy and lactation but only one conceived again. Thus, serious pituitary tumor complications are rare in hyperprolactinemic women with bromocriptine-induced pregnancies. The pregnancy does not worsen the condition. Resolution of hyperprolactinemia after bromocriptine-induced pregnancy is an infrequent finding. (Author abstract) (15 Refs)

7. HYPERPROLACTINEMIA IN MAN: CLINICAL INDICATIONS AND THERAPY.

Eversmann T, Eichinger R, Fahlbusch R, Rjosk HK, Von Werder K (c/o von Werder), Medizinische Klinik Innenstadt, Ziemssenstrasse 1, D-800 Munchen 2, W. Germany
Schweiz Med Wochenschr; 111(47):1782-1789 1981

Fifty-seven male patients with hyperprolactinemia have been investigated. Macroadenomas were found in 49 patients of whom 24 had received pituitary surgery before elevated PRL levels were discovered. In eight patients radiology of the pituitary fossa revealed either evidence of microadenoma or a completely normal sella turcica. Prolactin levels ranged from 582 to 498,000 uU/ml. All patients with macroprolactinomas, including those who had undergone previous surgery, had PRL levels above 5,000 uU/ml. Disturbances of libido and sexual potency were prevalent in the majority of patients, less frequently accompanied by gynecomastia and galactorrhea. However, visual disturbances were the reason for the first visit to the doctor in the majority of patients. Pituitary surgery led to improvement of visual field defects, though prolactin levels were never normalized. Postoperative radiotherapy had no significant influence on PRL levels. In contrast, bromocriptine therapy led, in the majority of patients not only to improvement of hypogonadal symptoms but also to normalization of PRL levels. (Author abstract) (28 Refs) (In GER)

8. THE PROLACTINOMA PROBLEM: LONG-TERM ISSUES AND SHORT-TERM ANSWERS.

Gold EM
No affiliation given
Conn Med; 45(11):701 1981

Incidence and recommended therapies for prolactinomas are discussed. High risk patients include women with amenorrhea and infertility, galactorrhea doubles tumor certainty. Early diagnosis is important, especially for women with a history of sustained estrogen exposure. Pituitary irradiation of prolactinomas is discouraged due to poor response rate. Bromocriptine mesylate therapy, while effective, is only recommended for symptomatic improvement of hyperprolactinemia in tumor-free patients or after unsuccessful surgery. Pituitary transsphenoidal microsurgery is the preferred treatment; successful removal of tumors, preservation of pituitary function in up to 90% of cases, and minimal mortality and morbidity rates may be obtained. (5 Refs)

9. ULTRASTRUCTURE OF PINEAL PARENCHYMAL NEOPLASMS.

Markesbery WR

Dept. Pathology, Univ. Kentucky Medical Center, Lexington, KY, 40506

Acta Neuropathol (Berl); 55(2):143-149 1981

Two cases of pineal neoplasm were examined by light and electron microscopy. Case 1 involved a 35-yr-old woman with headaches, dizziness, nausea, and gait disturbance. The tumor conformed to pineoblastoma and was characterized by a highly cellular, undifferentiated structure. Cells were small or medium-sized. The tumor contained Homer-Wright rosettes, capillary endothelial proliferation, multinucleated giant cells, and mitotic figures. Case 2 involved a 60-yr-old woman with headaches, a single syncopal episode, papilledema, impaired upward gaze, and unsteady tandem gait. The tumor was intermediate in character between pineocytoma and pineoblastoma and was marked primarily by small cells with occasional argyrophillic processes and Homer-Wright rosettes. Mitotic figures and other malignant features were absent. Calcification was present in the margin of part of the tumor. Cells in both tumors were characterized by prominent nuclei and scanty cytoplasm. Occasional cilia containing nine microtubule doublets without a central microtubule pair were found, as were astrocytic elements. (18 Refs)

THYROID TUMORS

10. B-SCAN SONOGRAPHY FOR TUMOR LOCALIZATION IN HYPERPARATHYROIDISM.

Kuhn FP, Gunther R, Wagner PK, Rothmund M, Thelen M

Institut f. Klin. Strahlenkunde, J. Gutenberg-Univ. Mainz, Langinbeckstr. 1, D-6500 Mainz, W. Germany

ROEFO; 135(4):412-416 1981

The value of sonography in preoperative localization of enlarged thyroid glands was investigated in 34 patients with primary, secondary, or tertiary hyperparathyroidism (HPT). Twenty-seven thyroid tumors were detected preoperatively through the use of this technique; 13 additional tumors were found at surgery. It was concluded that sonography is particularly valuable prior to surgical treatment of recurrences in patients with HPT. (21 Refs) (In GER)

11. ULM COLLECTION OF RARE TUMORS (III): WELL-DIFFERENTIATED FOLLICULAR THYROID CARCINOMA.

Fischer H, Baczako K
Abteilung Pathologie, Universitat Ulm, Oberer Eselsberg, 7900 Ulm/Donau, W. Germany
Aktuel Chir; 16(5):155-157 1981

Characteristics of primary, well-differentiated follicular thyroid carcinomas and their metastases are summarized. The absence of histological evidence of malignancy in these primary tumors is contrasted with their association with the development of distant metastases. These metastases are described with respect to localization, nature, course of development, and macro- and microscopic characteristics. Age and sex distributions of patients who develop such metastases are noted. Differentiation of metastases of well-differentiated follicular thyroid carcinoma from other malignancies (eg, papillary carcinoma) is examined. The association of metastasizing, well-differentiated follicular thyroid carcinoma with the presence of thyroid tissue in cervical lymph nodes is discussed, and different causes of this finding are examined. The good prognosis associated with surgical treatment of these primary tumors and their metastases is noted. (7 Refs) (In GER)

12. FAILURE OF CHEMOTHERAPY IN THYROID CANCERS.

Droz JP, Charbord P, Rougier P, Parmentier C
Departement de Medecine, Institut Gustave-Roussy, rue Camille-Desmoulins, F-94805 Villejuif Cedex, France
Bull Cancer (Paris); 68(4):350-352 1981

Twenty-seven patients with thyroid cancer underwent chemotherapy. Protocol A consisted of adriamycin (ADR: 40 mg) on day 1, VP 16 (100 mg) on day 2, and 5-fluorouracil (5-FU: 500 mg) and cyclophosphamide (CY: 400 mg) on days 3 and 4. In Protocol B, 40 mg/square meter of ADR was administered every 3 wk. Protocol C used the monthly administration of ADR (40 mg) on day 1, vincristine (1 mg) on day 2, and 5-FU (500 mg) on days 3, 4, and 5. Cis-platinum (90 mg/square meter) was administered every 3 wk in Protocol D. Of the 27 patients, 2 did not have a measurable tumor and 10 were physically able to receive only one chemotherapy cycle. Of the 15 evaluable patients (4 men, 11 women; 30-70 yr old), 7 had differentiated and 4 each had medullary and anaplastic carcinomas. All of the trials were considered failures. Only two regressions of less than 50% were observed. No notable drug toxicity (aplasia, fever, cardiotoxicity, and cochlear and renal pathology) was observed. No deaths resulted from chemotherapy. (5 Refs) (In FRE)

13. MISDIAGNOSES AND MISMANAGEMENT IN THYROID DISEASES.

Wenzel KW, Riedemann JH
Schilddrusenforschungsgruppe, Klinikum Steglitz der Freien Universitat Berlin, Berlin, W. Germany
Dtsch Med Wochenschr; 106(46):1526-1528 1981

Measures prior to diagnosis and treatment already installed were assessed retrospectively in 8,501 patients with suspect thyroid disease between the yr 1976 and 1979. In 10.5% of these patients there were 11.2% misdiagnosis or wrong treatment. The most common misdiagnoses were hyperthyroidism in euthyroid patients (1.9%), hypothyroidism in euthyroidism (0.8%), non-recognition or non-aspiration of cold nodules (0.9%), and missing a goiter (0.6%). Among diagnostic methods the radio-iodine test was most commonly the reason for a wrong diagnosis (66%). The TRH-test proved to be least erroneous, technical reasons being the cause of the 9.6% of misdiagnoses. The most common mismanagements were due to lack of prophylaxis of recurrence after goiter operation (1.5%), external irradiation of the thyroid gland with radium or R rays (0.7%), and during thyroid hormone treatment of goiter (1.3%). Iatrogenic disease existed mainly as factitious hyperthyroidism (0.7%), non-treated hypothyroidism after treatment with radio-iodine of hyperthyroidism (0.1%), and as goiter recurrence due to lack of prophylaxis of recurrence (0.8% of all patients). As every 10th patient was subjected to misdiagnosis or mismanagement, shifting to endocrinological advisory centers may prevent future mismanagement of thyroid disorders. (Author abstract) (no Refs) (In GER)

14. THE COMPARATIVE VALUE OF SERUM THYROGLOBULIN MEASUREMENTS AND IODINE 131 TOTAL BODY SCANS IN THE FOLLOW-UP STUDY OF PATIENTS WITH TREATED DIFFERENTIATED THYROID CANCER.

Ashcraft MW, Van Herle AJ
(c/o Van Herle) Dept. Medicine, Div. Endocrinology, UCLA Sch. Medicine, Los Angeles, CA, 90024
Am J Med; 71(5):806-814 1981

This study is an attempt to unify the evaluation of patients with well-differentiated thyroid cancer after ablative therapy. As such, serum thyroglobulin determinations on and off thyroid hormone (T4) therapy and iodine 131 total body scans were examined in 53 patient studies. No metastases were found in patients whose thyroglobulin value was undetectable (less than 1 ng/ml). Values during T4 thera py that were detectable, even as low s 4.2 ng/ml, were occasionally associated with metastases. After T4 withdrawal, thyroglobulin value and scan were obtained. Neither metastasis nor clinically detectable cancer was found in patients whose thyroglobulin value was less than 10 ng/ml while off T4. Conversely, a value greater than 10 ng/ml was often associated with documented metastases even when the scan was negative. In summary, a thyroglobulin value less than 1 ng/ml during T4 therapy or less than 10 ng/ml off T4 therapy suggests successful therapy and a routine scan could be avoided unless clinically indicated. However, a value greater than 10 ng/ml suggests the presence of metastasis despite a negative scan. Thyroglobulin determination substantially improves the management of these patients. (Author abstract) (45 Refs)

15. RADIOIMMUNOASSAY OF SERUM THYROGLOBULIN: TECHNIQUE AND CLINICAL RESULTS.

Benita G, Lapalus F, Bayer V, Bornet H, Hoch M
(c/o Lapalus) Dept. Nuclear Medicine, Centre Antoine-Lacassagne, 36 Voie Romaine, F-06054 Nice Cedex, France
Eur J Nucl Med; 6(11):515-520 1981

A double antibody radioimmunoassay using commercially available reagents for measuring human serum thyroglobulin (HTg) is described. Sera were obtained from 205 individuals, including 65 healthy controls, 69 cases of thyroid hypertrophy, 33 cases of Basedow's disease, and 38 cases of thyroid cancer. Preparation of reagents was limited to mixing buffers and labeling HTg with 125I. The level of detection was 2 ug/liter (l), with an 11% coefficient of variance for interassay reproducibility. The normal HTg value was 33.0 +-21.20 ug/l. Patients with goiters and cold nodules showed values of 80.9 +-57.1 ug/l. Patients with Basedow's disease exhibited values similar to this group. Of patients treated for thyroid cancer, those with no sign of recurrent disease had low or undetectable levels of HTg. Patients with metastatic disease showed values of 100-400 ug/l. Results indicate that serum HTg is a useful indicator for monitoring differentiated thyroid cancers which reduces dependence on techniques that interrupt therapy or involve radiation hazard. (9 Refs)

PARATHYROID TUMORS

16. COMPUTED TOMOGRAPHY FOR LOCALIZATION OF PARATHYROID ADENOMAS.

Whitley NO, Bohlman M, Connor TB, McCrea ES, Mason GR, Whitley JE
Dept. Diagnostic Radiology, Univ. Maryland Hosp., 22 South Greene St., Baltimore, MD, 21201
J Comput Assist Tomogr; 5(5):812-817 1981

Fourteen consecutive patients with the clinical diagnosis of primary hyperparathyroidism had computed tomography (CT) preoperatively to evaluate the use of CT in localizing parathyroid adenomas. The patients were scanned from above the level of the thyroid cartilage to the bifurcation of the trachea. Computed tomography correctly identified, prospectively, the site of the adenoma in 7 of 14 patients, including one adenoma that was ectopic in location. Nine of these patients also had barium esophagrams, and this study was accurate in only three of the nine. Our study suggests that CT may be beneficial in the preoperative localization of parathyroid adenomas, particularly those in ectopic locations. (Author abstract) (10 Refs)

17. HIGH-RESOLUTION REAL-TIME SONOGRAPHY OF THE PARATHYROID.

Simeone JF, Mueller PR, Ferrucci JT, VanSonnenberg E, Wang CA, Hall DA, Wittenberg J
Dept. Radiology, Massachusetts General Hosp., Boston, MA, 02114
Radiology; 141(3,part1):745-751 1981

High-resolution real-time sonography was performed in 45 patients with the clinical diagnosis of hypercalcemia and suspected hyperparathyroidism. There were 35 true positives, 4 false positives, 5 false negatives and 1 true negative. The sensitivity of the technique was 88%, the specificity was 96%, and the predictive value was 90%. Sonography is the procedure of choice for localization of the enlarged parathyroid gland before the neck is surgically explored. (Author abstract) (7 Refs)

18. SURGICAL ASPECTS OF PRIMARY HYPERPARATHYROIDISM.

Heslinga JM
Dept. Surgery, Univ. Hosp., State Univ., Leyden, The Netherlands
Neth J Surg; 33(4):200-205 1981

The preoperative findings and surgical results of 217 operations for primary hyperparathyroidism (PH) were studied. PH occurred more often in women than men. Three or more glands were found in 89% of cases. A discrepancy was noted between histological confirmation of hyperplasia (50%) and surgically observed gland enlargement (70%). Surgery was successful in 96% of cases. No major complications were noted. (16 Refs)

19. PRIMARY HYPERPARATHYROIDISM: CHANGING CLINICAL SPECTRUM, PREVALENCE OF HYPERTENSION, AND DISCRIMINANT ANALYSIS OF LABORATORY TESTS.

Lafferty FW
1611 S. Green Road, South Euclid, OH, 44121
Arch Intern Med; 141(13):1761-1766 1981

The clinical spectrum of 100 consecutive cases of surgically proved primary hyperparathyroidism treated from 1974 through 1978 was analyzed. Their laboratory test results were compared with 64 cases of other forms of hypercalcemia using multivariate discriminant analysis. The clinical spectrum has dramatically shifted during the past three decades from renal calculi and bone disease to the asymptomatic patient discovered by routine serum chemical analysis. Hypertension was twice as common among hyperparathyroid patients as in the general population but failed to improve in 92% after parathyroidectomy. The most useful discriminant laboratory tests in descending order of value were the serum chloride, serum calcium, hematocrit, serum phosphorus, and parathormone. Multivariate discriminant analysis of the serum calcium, phosphorus, chloride, and Hct provided a 98% degree of accuracy in separating hyperparathyroidism from other forms of h ypercalcemia. (Author abstract) (29 Refs)

ADRENAL TUMORS

20. CLINICAL AND LABORATORY FINDINGS AND RESULTS OF THERAPY IN 58 PATIENTS WITH ADRENOCORTICAL TUMORS ADMITTED TO A SINGLE MEDICAL CENTER (1951 TO 1978).

Bertagna C, Orth DN
Div. Endocrinology, Vanderbilt Univ. Medical Center North, Room A-4215, Nashville, TN, 37232
Am J Med; 71(5):855-875 1981

We reviewed 150 findings in 58 patients (14 males and 44 females) with adrenocortical tumors (26 with adenoma and 32 with carcinoma) admitted to Vanderbilt Hospital during 28 yr. In general, our findings agree with those reported by others in multi-institutional series or literature reviews. Adenomas took longer to diagnose than carcinomas. Adenomas usually caused Cushing's syndrome, but two caused virilization and three caused no endocrine syndrome. There was no difference in time required for diagnosis of carcinoma in men or women or in those with Cushing's syndrome, virilization or no endocrine syndrome. Urinary 17-hydroxycorticoid (17-OHCS) levels were similar in those with adenoma and those with carcinoma, but 17-ketosteroid (17-KS) levels were usually less than 20 mg per day in patients with adenoma and greater than 20 mg per day in patients with carcinoma. Adenomas were uniformly independent of endogenous ACTH stimulation, but frequently responded to exogenous ACTH. As with adenomas, no carcinoma demonstrated normal suppression with dexamethasone or normal response to metyrapone, but only one responded to exogenous ACTH. Some patients had no clinical Cushing's syndrome despite high levels of plasma cortisol and urine 17-OHCS. 'Nonfunctional' tumors probably merely secreted insufficient steroids to cause signs and symptoms. Patients with adenoma were uniformly cured by surgical tumor resection. Occasional patients with carcinoma enjoyed long survival despite incomplete resection of their tumors, but most patients died of recurrent or metastatic carcinoma within 7 yr, often within a yr or two. Small tumor size and benign histologic features were insufficient to predict benign clinical behavior. The adrenocorticolytic drug, o,p'DDD, offered objective remission for only an occasional patient. (Author abstract) (37 Refs)

21. RESIDUAL ADRENOCORTICAL FUNCTION AFTER BILATERAL 'TOTAL' ADRENALECTOMY FOR CUSHING'S DISEASE.

Chalmers RA, Mashiter K, Joplin GF
(c/o Joplin) Endocrine Unit, Dept. Medicine, Royal Postgraduate Medical Sch., Hammersmith, London W12 0HS, England
Lancet; 2(8257):1196-1199 1981

Six patients who had been treated for pituitary-dependent Cushing's syndrome by intended complete removal of the adrenal glands are described. There were clinical grounds for attempting to reduce maintenance steroid therapy in each case, and it was found possible to withdraw steroids completely without adverse effects. These findings illustrate the importance of clinically assessing the minimum steroid requirements of adrenalectomized patients and the need for continued surveillance for persistent or recurrent Cushing's syndrome. (Author abstract) (21 Refs)

22. SERUM GASTRIN LEVELS IN PATIENTS WITH PHEOCHROMOCYTOMA.

Sagara K, Oishi S, Umeda T, Sato T
Third Dept. Internal Medicine, Kumamoto Univ. Medical Sch., 1-1-1 Honsho, Kumamoto 860, Japan
Jpn J Clin Oncol; 11(2):363-366 1981

The clinical significance of serum gastrin levels was investigated in 11 pheochromocytoma patients, 26 essential hypertension patients, and 20 healthy controls. There were no significant differences in either epinephrine or norepinephrine excretion between normal controls and hypertensive patients, while pheochromocytoma patients showed abnormally high secretion of epinephrine or norepinephrine or both. Abnormally high serum gastrin levels in pheochromocytoma patients returned to normal after resection of the tumor. Epinephrine was found to affect serum gastrin levels to a greater extent than norepinephrine. High serum gastrin levels were found in patients bearing epinephrine-secreting tumors. Normal gastrin levels were observed in patients with extra-adrenal tumors. Assay of serum gastrin levels in patients about to undergo surgical resection of pheochromocytoma may aid in location of the tumor. (11 Refs)

23. PATHOMORPHOLOGICAL CHANGES IN THE MYOCARDIUM AND THE CORONARY VESSELS IN PATIENTS WITH ADRENAL PHEOCHROMOCYTOMA.

Lebedevskaia VP
Dept. Pathology and Forensic Medicine, State Univ., Uzhgorod, USSR
Arkh Patol; 43(9):26-30 1981

Results of autopsy examination of the myocardium and of coronary vessels in seven patients (6 men, 1 woman; 37-56 yr old) with adrenal pheochromocytoma are reported. Intravitally, the disease was misdiagnosed as hypertonic disease in five of the patients and as myocardial infarction in two. Atherosclerosis of the coronary arteries was observed in four of the patients. Mild hypertrophy of the left heart ventricle and dystrophy of the myocardium were detected in all seven of the patients. The most marked changes were observed in the microcirculation network. (18 Refs) (In RUS)

24. SUPRARENAL MASS AND ITS DIFFERENTIAL DIAGNOSIS.

Siekavizza JL, Bernardino ME, Samaan NA
Dept. Medicine, Section Endocrinology, Univ. Texas Cancer Center M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Urology; 18(6):625-632 1981

Nine cases of suprarenal masses without endocrine abnormalities are presented: two adrenal pseudocysts, two adrenal myelolipomas, two neuroblastomas, one lymphoma metastatic to the adrenal glands, one teratoma, and one adrenal cortical carcinoma metastatic to the contralateral gland. The clinical and radiologic findings are discussed. Noninvasive and invasive procedures and their usefulness in diagnosing masses in the suprarenal area are reported. The importance of metastases to the adrenal glands in the differential diagnosis of suprarenal masses was investigated by reviewing the autopsies done from January through June, 1979, at the University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, Houston, Texas. Adrenal metastases were found in 26% of the cases studied. Breast and lung carcinomas and lymphomas were the most commonly found neoplasia. The relative incidence of microscopic and macroscopic metastases in all patients with tumor is discussed. (Author abstract) (30 Refs)

PANCREAS TUMORS

25. INSULINOMA.

Zhang Z, Lu H
Dept. Surgery, Bethune Medical Coll., Jilin, People's Republic of China
Zhonghua Yixue Zazhi; 60(4):205 1981

Diagnosis and surgical treatment are described for 25 cases of insulinoma seen between 1965 and 1978. Tumor sizes ranged from 0.8 cm in diameter to 13 x 9 x 7 cm. Surgical results were satisfactory. Among the 24 cases of preoperative hypoglycemia in this series, only 1 case still had hypoglycemia symptoms after surgery, which was controlled by further resection of the pancreas and diet. The diagnosis of insulinoma and its differential diagnosis from hypoglycemia epilepsy and neurosis are discussed. (no Refs) (In CHI)

OTHER TUMORS OF GLANDULAR TISSUES

26. SOME ASPECTS OF THE ENDOCRINE STATUS IN THE INFLAMMATORY BREAST CARCINOMA (MASTITIS CARCINOSA).

Kiricuta I, Frenkel Z
(c/o Frenkel), Inst. Oncology, Str. Republicii 34-36, 3400 Cluj-Napoca, Romania
Arch Geschwulstforsch; 52(1):67-73 1982

Endocrine parameters in 87 patients with inflammatory breast carcinoma (IBC) of rapid evolution (Group I) were compared with those in 400 patients with noninflammatory breast carcinoma (NBC) of normal evolution (Group II). Total urinary estrogens were measured in 81 patients from Group I and in 326 patients from Group II. Urinary 17-ketosteroids were measured in 60 patients from Group I and 61 patients from Group II. Mean age at menarche was significantly higher (14.8 +-0.22 yr) in Group I than in Group II (14.0 +-0.06 yr). Menarche at 16 yr or later occurred in 36.8% of Group I compared with 16.75% of Group II. Mean number of abortions was lower in Group I (1.72) than in Group II (2.16). Cases with no abortions were more frequent (48.1%) in Group I than in Group II (41.7%). Mean levels of urinary ethiocholanolone (Et) were low in Group I (0.66 +-0.04 mg/24 hr) than in Group II (1.04 +-0.08 mg/24 hr). The androsterone/Et ratio was higher (1.00) and the Et/11-oxygenated-17-ketosteroids ratio was lower (0.72) in group I than in group II (0.75 and 0.91, respectively). Results indicate a greater hormonal imbalance in IBC than in NBC. (49 Refs)

27. TREATMENT OF ADVANCED BREAST CANCER WITH PROGESTINS. A REVIEW.

Lober J, Rose C, Salimtschik M, Mouridsen HT
(c/o Mouridsen) Dept. RA-R 6, Finsen Inst., 49, Strandboulevarden, DK - 2100 Copenhagen O, Denmark
Acta Obstet Gynecol Scand [Suppl]; (101):39-46 1981

This paper reviews the theoretical background for the use of progestins in advanced breast cancer and the clinical experience obtained from 13 major studies. the av rate of response is about 30%, with somewhat higher rates when the dominant site of disease is localized to soft tissue and to bones, compared with viscera. Furthermore it seems that cross resistance between progestin therapy and other endocrine therapies is only partial. However, response rates related to previous therapy and to important prognostic variables such as age of the patient, disease-free interval and hormone receptor content of the tumor tissue are poorly elucidated. Only limited data are available concerning response rate in relation to dose and route of administration and data from prospective randomized trials to analyze these relations are still lacking. Considering the only modest side effects of treatment with progestins and the clinical and theoretical evidence favoring a mode of action different from that of other endocrine therapies, progestins are drugs with interesting qualities. Therefore future controlled studies with progestins alone or in combination with other systemic therapies should be carried out to establish the therapeutic efficacy of progestin therapy in primary and advanced disease. (Author abstract) (68 Refs)

28. TAMOXIFEN VERSUS AMINOGLUTETHIMIDE IN ADVANCED BREAST CARCINOMA: A RANDOMISED CROSS-OVER TRIAL.

Smith IE, Harris AL, Morgan M, Ford HT, Gazet JC, Harmer CL, White H, Parsons CA, Villardo A, Walsh G, McKinna JA
Breast Unit, Royal Marsden Hosp., London SW3 6JJ, England
Br Med J; 283(6304):1432-1434 1981

Altogether 117 patients with advanced breast cancer were treated with either tamoxifen 10 mg by mouth bid or aminoglutethimide 250 mg by mouth 4x daily with hydrocortisone 20 mg bid in a randomized cross-over trial in which patients who failed to respond to the first treatment or relapsed while receiving it were switched to the other. Eighteen (30%) out of 60 patients initially treated with tamoxifen achieved an objective response and 11 (18%) showed stable disease. Seventeen (30%) out of 57 patients treated initially with aminoglutethimide achieved an objective response and 13 (23%) achieved stable disease. Objective responses in bone metastases were achieved more commonly with aminoglutethimide (11 patients (35%)) than with tamoxifen (5 (17%)). The predicted median duration of response for tamoxifen was 15 mo and for aminoglutethimide over 15 mo (no significant difference). Five (15%) out of 34 patients who failed to resp ond to tamoxifen and four out of six patients who relapsed after responding to tamoxifen subsequently responded to aminoglutethimide. In contrast, only 2 (6%) out of 31 patients who failed to respond to aminoglutethimide and none out of four patients who relapsed while receiving aminoglutethimide subsequently responded to tamoxifen. The main side effects occurring in the 97 patients who received aminoglutethimide as first- or second-line treatment were lethargy and drowsiness (36 patients) and rash (29); seven patients had to stop treatment because of side effects. In contrast, side effects were rare and mild with tamoxifen and no patient had to stop treatment because of them. Both tamoxifen and aminoglutethimide appear from this study to be equally effective in the medical endocrine treatment of advanced breast cancer. (Author abstract) (8 Refs)

29. A STUDY OF ESTROGEN AND PROGESTERONE CYTOSOL RECEPTOR CONCENTRATION IN BENIGN AND MALIGNANT OVARIAN TUMORS AND A REVIEW OF MALIGNANT OVARIAN TUMORS TREATED WITH MEDROXYPROGESTERONE ACETATE.

Bergqvist A, Kullander S, Thorell J
Dept. Obstetrics and Gynecology, Malmo Allmanna Sjukhus, S - 214 01 Malmo, Sweden
Acta Obstet Gynecol Scand [Suppl]; (101):75-81 1981

ER and PR were assayed in 13 malignant and 20 benign ovarian tumors of different histologic types. ER was detectable in 67% and PR in 40% of the malignant tumors, compared with 35 and 45% in the benign tumors, respectively. The ER concentration was somewhat higher in the malignant lesions but there was no difference in the PR level. A retrospective review of 39 primary ovarian tumors of different pathologic stages and classes, treated postoperatively with medroxyprogesterone acetate (MPA, Depo-Provera, Upjohn) and in most cases Melphalan, showed a high Karnofsky performance index and good complete and partial response rates. The need for a prospective, controlled study of the role of MPA treatment of malignant ovarian tumors is evident. (Author abstract) (33 Refs)

30. CYTOSOL ESTROCEN AND PROGESTERONE RECEPTORS IN NORMAL AND PATHOLOGICAL TISSUES OF THE HUMAN UTERUS AND OVARIES.

Baron J, Chwalisz K, Mikolajewska-Fischer Z, Adamski J
Klinika Endokrynologii Ginekologicznej, Instytut Ginekologii i Poloznictwa AM, ul. Polna 33, 60-535 Poznan, Poland
Ginekol Pol; 52(7):585-590 1981

Cytosol estrogen receptor (ER) and progesterone receptor (PR) levels were determined in normal and pathological tissues from endometria and ovaries. The samples were obtained from 30 women with normal endometrium, 20 women with normal myometrium, 10 women with normal ovaries, from 15 patients with endometrial carcinoma, 25 patients with uterine myoma, and 8 patients with ovarian neoplasms. The ER levels av (in femtomoles/mg) 193.4 in the follicular phase, 96.1 in the luteal phase, 166.7 in the climacterium (endometrium); 55.2 in the reproductive period and 49.3 in the climacterium in the myometrium, 22.1 in the normal ovaries, 160.6 in the patients with endometrial carcinoma (av age 62.2 yr), 104.5 in myoma (av age 43.9 yr), and 0-2,000 in ovarian neoplasms. The PR levels av 302.5 in the follicular phase, 125.2 in the luteal phase, 257 in the climacterium in the normal endometrium; 161.8 in the reproductive age and 121.4 in the climacterium in the normal myometrium; 67.1 in the normal ovaries; 131.5 (9-735) in endometrial carcinoma, 286 (0-705) in myoma, and 27-4,000 in ovarian neoplasms. The findings indicate the value of the determination of ER and PR levels in cytosol to evaluate the resistance of the target tissue to hormone therapy. (25 Refs) (In POL)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

31. CYCLICAL COMBINATION CHEMOTHERAPY AND THYROID FUNCTION IN PATIENTS WITH ADVANCED HODGKIN'S DISEASE.

Sutcliffe SB, Chapman R, Wrigley PF
Dept. Radiation Oncology, Princess Margaret Hosp., 500 Sherbourne St., Toronto, Ontario, M4X 1K9, Canada
Med Pediatr Oncol; 9(5):439-448 1981

Clinical and biochemical assessment of thyroid function was undertaken in patients with Hodgkin's disease at designated points following diagnosis. At diagnosis, 2 of 20 patients had either abnormally low routine thyroid indices, or elevated thyroid stimulating hormone (TSH) levels that were not due to iodine-based investigations. Following lymphography, 76.5% of patients had TSH levels that remained elevated for a median period of 3 mo. No detectable thyroid dysfunction was induced during chemotherapy. Fifty-four patients were studied at a median time of 35 mo after chemotherapy. One euthyroid patient had a nodular goiter, and one had abnormal thyroid indices. TSH levels were elevated in 44% of patients, although the median TSH level for the group was normal. Half the patients had abnormal TRH stimulation tests. Sixty patients were studied after irradiation and chemotherapy. Four patients had clinical thyroid dysfunction, and 10% of routine thyroid indices were abnormal. TSH levels were abnormal in 80%, with a markedly elevated median level. All thyroid releasing hormone stimulation tests were abnormal. (Author abstract) (28 Refs)

32. SUMMARY OF WORKSHOP ON PRESENT KNOWLEDGE OF LATE EFFECTS OF TREATMENT ON ENDOCRINE FUNCTION.

Sklar C, Nesbit M
Dept. Pediatrics, Mayo Memorial Building, Univ. Minnesota, Minneapolis, MN, 55455
Cancer Clin Trials; 4(Suppl):21-23 1981

The late effects of radiation and drug treatment on the pituitary, hypothalamus, thyroid, and gonads are reviewed. Damage to the hypothalamus at doses of 3,000-5,000 rad is reflected in a high rate of growth hormone deficiency. Children who have received greater than 2,500 rad to the hypothalamic pituitary area for treatment of cancer should be evaluated for siting and standing height every 6 mo for 3 yr after treatment. Thyroid dysfunction occurs in 40-80% of patients following head and neck irradiation. All patients treated with greater than 2,000 rad to the thyroid region should be studied every 6 mo for 2 yr, and then yearly. The alkylating agents are the major drugs responsible for cytotoxic-induced gonadal damage which appears to be a function of both sex and age. Spermatogenesis in the adult male is most sensitive to the toxic effect of chemotherapy. For post-treatment follow-up, gonadotropin and sex steroids levels should be measured every 6 mo for 2 yr. Future areas of investigation should include studies on the pituitary, hypothalamus, thyroid, testis, ovary, and other endocrine organs, especially the adrenal and pancreas after cancer treatment. (10 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

33. ADRENERGIC AND DOPAMINERGIC MODULATION GROWTH HORMONE AND PROLACTIN SECRETION IN NORMAL AND TUMOR-BEARING HUMAN PITUITARIES IN MONOLAYER CULTURE.

Tallo D, Malarkey WB
(c/o Malarkey), Ohio State Univ. Hosp., 410 West Tenth Ave., Columbus, OH, 43210
J Clin Endocrinol Metab; 53(6):1278-1284 1981

Adrenergic and dopaminergic agonists administered in vivo stimulate GH secretion and inhibit PRL release. To investigate the direct effect of these agents on GH and PRL secretion from normal and tumor-bearing human pituitaries, they were added to monolayer cultures of surgically obtained pituitary tissue from patients with metastatic breast carcinoma, prolactinoma, and acromegaly. This study demonstrates that adrenergic and dopaminergic agonists directly inhibit normal human pituitary PRL and GH secretion. These findings are in contrast to the known in vivo GH stimulatory effect of these agents in man, which suggests that dopaminergically induced GH release may be mediated via the hypothalamus or higher central nervous system centers. In addition, dopaminergic defects exist in the adenomatous somatotrophs and lactotrophs of some patients with pituitary tumors. (36 Refs)

34. BROMOCRIPTINE SUPPRESSES ACTH SECRETION FROM HUMAN PITUITARY TUMOUR CELLS IN CULTURE BY A DOPAMINERGIC MECHANISM.

Adams EF, Ashby MJ, Brown SM, White MC, Mashiter K
(c/o Mashiter) Dept. Medicine, Royal Postgraduate Medical Sch., Hammersmith Hosp., Du Cane Road, London W12 0HS, England
Clin Endocrinol (Oxf); 15(5):479-484 1981

The effect of bromocriptine (BCR) on ACTH secretion from cell cultures of a human corticotropic adenoma and an ectopic ACTH secreting carcinoid tumor of the lung was examined. BCR (0.13-13.0 uM) significantly inhibited ACTH secretion in a dose-dependent manner when added to cultures of the corticotropic adenoma for 24 hr. The adenoma originated in a woman with Nelson's syndrome. BCR did not affect ACTH secretion from cells of lung carcinoid under identical conditions. BCR (1.3 uM) suppressed ACTH secretion from pituitary adenoma cells in a second experiment; the suppression was blocked by co-incubation of cells with haloperidol (HAL). HAL alone had no effect. Varying doses (0.013-13.0 uM) of serotonin or metergoline did not affect pituitary adenoma cell ACTH secretion during a 4 hr period, and 13.0 uM serotonin did not change BCR suppression during a 24 hr incubation. Dopamine (10.0 uM) significantly inhibited ACTH secretion from the pituitary adenoma cells during a 4 hr incubation, whereas lower doses had no effect. Results demonstrate a direct suppressive action of BCR on a human pituitary corticotropic adenoma through dopaminergic rather than serotoninergic mechanisms. (12 Refs)

35. STIMULATION OF GROWTH HORMONE RELEASE BY VASOACTIVE INTESTINAL POLYPEPTIDE FROM HUMAN PITUITARY ADENOMAS IN VITRO.

Matsushita N, Kato Y, Katakami H, Shimatsu A, Yanaihara N, Imura H

Dept. Medicine., Second Medical Clinic, Kyoto Univ. Faculty Medicine, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606, Japan

J Clin Endocrinol Metab; 53(6):1297-1300 1981

The effects of vasoactive intestinal polypeptide (VIP), TRH, dopamine, and rat median eminence extract on GH release from GH-secreting pituitary adenomas were studied in vitro using a sensitive superfusion method. Dispersed pituitary tumor cells obtained from three patients with acromegaly were placed in a superfusion column, and the amounts of GH in the superfusate were determined. The addition of VIP (10(-6) M) to the perfusion system resulted in a marked increase in GH release in all three cases, and a dose-response relationship in VIP (10(-8) -10(-6) M)-induced GH secretion was observed in one case studied. TRH (10(-7) M) and median eminence extract (1 equivalent/ml) also caused an abrupt and marked increase in GH release in all of the experiments. The infusion of either dopamine (10(-7) M) or bromocriptine (10(-7) M) inhibited GH secretion. These results suggest that VIP as well as TRH stimulate GH secretion by a direct action on GH-secreting pituitary tumor cells in at least some acromegalic patients. (Author abstract) (23 Refs)

36. ESTROGEN INDUCED GROWTH OF HUMAN BREAST CANCER CELLS (MCF-7) IN ATHYMIC NUDE MICE IS ENHANCED BY SECRETIONS FROM A TRANSPLANTABLE PITUITARY TUMOR.

Welsch CW, Swim EL, McManus MJ, White AC, McGrath CM

Dept. Anatomy, Michigan State Univ., East Lansing, MI, 48824

Cancer Lett; 14(3):309-316 1981

The influence of pituitary hormones on growth of MCF-7 human breast tumor cells maintained in athymic nude mice was investigated. Sc injection of a pellet containing 17B-estradiol, and estrone in drinking water (0.5 mg/liter), resulted in sustained growth of the cells. Injection of a prolactin/g rowth hormone secreting rat pituitary tumor into the estrogen treated mice also caused growth of the tumor cells. No growth of tumor cells was observed in animals injected with pituitary tumor alone or in animals receiving neither pituitary tumor nor estrogen. Thus, rat pituitary tumor secretions enhanced the rate of in vivo MCF-7 tumor growth in estrogen treated animals, suggesting a synergism in their respective actions. (16 Refs)

37. EFFECTS OF ESTROGENS AND ANTIESTROGENS ON ESTROGEN RECEPTOR DYNAMICS AND THE INDUCTION OF PROGESTERONE RECEPTOR IN MCF-7 HUMAN BREAST CANCER CELLS.

Eckert RL, Katzenellenbogen BS
(c/o Katzenellenbogen) Sch. Basic Medical Sciences, Univ. Illinois Coll. Medicine, Urbana, IL, 61801
Cancer Res; 42(1):139-144 1982

Antiestrogens appear to be useful in the treatment of endocrine-responsive breast cancers in humans. We have examined the effects of estrogens (estradiol and diethylstilbestrol), and antiestrogens with a range of affinities for estrogen receptor (ER), on intracellular ER dynamics and biological response (progesterone receptor) induction in MCF-7 human breast cancer cells. The triphenylethylene antiestrogens studied are alpha- *p-[2-(1-pyrrolidino)ethoxy]phenyl* -4-methoxy alpha'-nitrostilbene (Cl628), alpha- *p-[2-(1pyrrolidino)ethoxy]phenyl* -4-hydroxy alpha'-nitrostilbene, cis- *3-[p-(1,2,3,4,-tetrahydro-6-methoxy-2-phenyl-1 naphthyl)phenoxy]-1,2-propanediol* , and cis-*3-[p-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1 naphthyl)phenoxy]-1,2,propanediol. The results indicate that: (a) ER translocation to the nucleus and progesterone receptor induction appear to be related to ligand affinity; (b) antiestrogens can differ substantially from one another in their dynamics of interaction with ER and in their abilities to stimulate increases in cellular progesterone receptor; (c) processing of ER by antiestrogens such as C1628 does not ensure subsequent induction of progesterone receptor; and (d) an apparently complex relationship exists between the presence and duration of hormone receptor complexes in the nucleus and the induction of progesterone receptor in MCF-7 cells. Since all four antiestrogens inhibit MCF-7 cell growth but differ in their ability to increase cellular progesterone receptor levels, these studies indicate that growth and progesterone receptor induction are phenomena that are independently modulated by antiestrogens in these human breast cancer cells. (36 Refs)*

38. INVESTIGATIONS ON HORMONE DEPENDENCY OF HUMAN MAMMARY CARCINOMAS TRANSPLANTED INTO NUDE MICE.

Brunner N, Spang-Thomsen M
Univ. Inst. Pathological Anatomy, 11, Frederik V's vej, DK-2100 Copenhagen, Denmark
Acta Obstet Gynecol Scand [Suppl]; (101):37-38 1981

Since human mammary cancer can be transplanted into nude mice, this makes possib le the in vivo study of relations between hormone dependency and the steroid hormone receptor content of the tumors. The macroscopic growth curve of the transplanted tumors during endocrine therapy will reflect the hormone dependency. The results can be compared with successive steroid hormone receptor determinations in the tumor tissue. (Author abstract) (8 Refs)

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. DIAGNOSIS OF TUMORS OF THE PITUITARY REGION WITH TWO-PLANE CT SCANS WITH SPECIAL REFERENCE TO OPERATIVE INDICATION FOR THE TRANSSPHENOIDAL APPROACH.

Murata M, Inoue H, Misumi S, Shimizu T, Tamura M, Kawafuchi J
Dept. Neurosurgery, Gunma Univ., Maebashi 371, Japan
Neurol Med Chir (Tokyo); 21(8):863-871 1981

Thirty-five cases of tumors of the pituitary region were analyzed with two-plane computed tomography (ordinary and reverse sections) and classified into six types. Ordinary sections were examined at + 25 degrees from Reid's base line, and reverse sections were examined at -20 degrees from Reid's base line with an Electronic Music Industries 1010. Histologically, the pituitary adenomas included 16 chromophobe adenoma, 6 mixed adenoma, 3 eosinophilic adenoma, 7 craniopharyngiomas, 1 Rathke's cleft cyst, 1 granuloma, and 1 neuroblastoma. On the basis of degree of extension and direction of growth, tumors were classified as Type I (intrasellar tumor), Type II (extension into the chiasmatic cistern), Type III (suprasellar extension compressing the third ventricle up to the foramen of Monro), Type IV (suprasellar extension beyond the foramen of Monro), Type V (parasellar extension), or Type VI (extending upward and compressing the lateral ventricle). Small tumors were more easily detected with the reverse than with the ordinary section. All craniopharyngiomas were Types III-VI. Subnasal transsphenoidal approach was performed to remove Type I-III tumors and to decompress the optic nerve in cases (Type IV tumors) of old patients or patients with severe complications. (30 Refs) (In JPN)

2. TRANSSPHENOIDAL MICROSURGERY FOR PROLACTIN-SECRETING PITUITARY ADENOMAS: RESULTS IN 100 WOMEN WITH AMENORRHEA-GALACTORRHEA SYNDROME.

Faria MA, Tindall GT
Section Neurological Surgery, Emory Univ. Clinic, 1365 Clifton Road, N.E., Atlanta, GA, 30322
J Neurosurg; 56(1):33-43 1982

The authors present the results of transsphenoidal microsurgery in 100 women with the amenorrhea-galactorrhea syndrome caused by pituitary adenomas associated with hyperprolactinemia (prolactinomas). As the surgical results were closely related to the preoperative levels of serum prolactin, the patients were divided into two groups: Patients with preoperative prolactin less than 200 ng/ml (Group 1), and those with preoperative prolactin greater than 20 mg/ml (Group 2). The results in Group 1 (72 patients) were significantly better. In this group 56 (78%) patients regained normal menstrual cycles, and 55 (76%) had return of elevated prolactin levels to normal following surgery. In Group 2 (28 patients), however, only 11 (39%) resumed normal menstrual periods postoperatively, and 13 (46%) had return of elevated prolactin levels to normal. There was good correlation between tumor size and the preoperative level of prolactin. Of the 72 women in Group I, 58 (81%) had tumors less than 1 cm (microadenomas), whereas of the 28 women in Group 2, only 4 (14%) had tumors of that size. All patients with visual field deficits preoperatively improved or had a normal visual examination postoperatively; none was made worse by surgery. Four patients (3 in Group 2) have required additional surgery and/or irradiation. In the last six patients of the series, contrast-enhanced coronal computerized tomography slices made with the updated General Electric scanner detected five m icroadenomas. Considering that a relatively high percentage of sellar polytomograms are negative in patients with proven microadenomas (that is, only 40 of 72 patients in Group 1 had abnormal polytomography), it is likely that sellar polytomography will significantly decrease in importance in the diagnostic work-up of these patients. The authors provide a rationale for transsphenoidal microsurgery in these patients as opposed to other forms of management, such as bromocriptine therapy and irradiation. (Author abstract) (58 Refs)

3. TRANSSPHENOIDAL MICRONEUROSURGERY - PART 3. THE MORPHOLOGY AND ENDOCRINOLOGICAL CURE OF FUNCTIONING ADENOMAS.

Oi S, Ciric IS, Kerr WD, Guthrie FW, Murphy ED
Dept. Neurosurgery, Kobe Univ., Kobe 650, Japan
Neurol Med Chir (Tokyo); 21(9):955-960 1981

Sixty-three pituitary functioning adenomas were analyzed with respect to correlation between the preoperative morphological/endocrinological potentials of the tumor and the postoperative surgical endocrinological cure rates. There were 38 prolactin, 18 growth hormone and 7 ACTH secreting adenomas. In 38 prolactin secreting adenomas, 16 were microadenomas. A trial of selective total adenomectomy completely preserving the normal pituitary gland was performed in eight cases. The endocrinological cure rate (50%) and the absence of galactorrhea (50%) were not satisfactory. Attempted complete adenomectomy with a partial hypophysectomy resecting some normal surrounding tissue improved the cure rates to 87%. Large tumors with sella destruction or tumors with a very high preoperative serum prolactin (not always correlated) had poor endocrinological cure rates. The endocrinological cure rate was 30% in the prolactin secreting adenomas with grade III and IV sella turcica (Hardy and Vezina classification). The rate was 40% in the prolactinomas with high preoperative endocrinological potentials (over 500 ng/ml), while it was 80% in the tumors with preoperative serum prolactin of less than 100 ng/ml. Similar results were obtained in the analysis of growth hormone secreting adenomas. The necessity of postoperative hormonal replacement increased in the larger tumors, 30% in Grades I and II and 50% in Grades III and IV. The hormonal cure rate was 80% in tumors with a preoperative growth hormone level of less than 100 ng/ml and 38% in those with over 100 ng/ml. The majority of ACTH secreting tumors were microadenomas and had excellent cure rates, 86% in seven cases. This study strongly suggests that the preoperative morphological/endocrinological potentials are the major factors affecting the postoperative surgical endocrinological cure rates in functioning adenomas. The authors emphasize that the transsphenoidal resection of the pituitary adenomas should be performed while the tumors have low morphological/endocrinological potentials to obtain excellent surgical results. (Author abstract) (19 Refs) (In JPN)

4. SURGICAL TREATMENT OF CUSHING'S DISEASE.

Basso A, Guitelman A, Belli S, Carrizo A, Berner S
Ayaguche 1342-PB, Buenos Aires, Argentina
Neurochirurgie; 27(3):173-179 1981

The evaluation, treatment, and course of Cushing's disease in 23 patients are reported. Patients presented with hypercortisolism and received hormonal and radiographic evaluations. Elevated levels of urinary metabolites and an aberrant rhythm of cortisol production were the most common findings. In 19 patients, radiographs revealed a deformed sella. In 15/21 patients, intrapituitary adenomas were found during surgery. The transphenoidal approach was used to perform total hypophysectomy in six patients. In 5/6 of these patients, histological investigation of the surgical specimen revealed adenomas. Post-operative radiotherapy was given to nine patients. Among the 21 patients who underwent surgery, only three failures were observed. (35 Refs) (In FRE)

5. EXPERIENCE WITH SELECTIVE VENOUS SAMPLING IN DIAGNOSIS OF ACTH-DEPENDENT CUSHING'S SYNDROME.

Drury PL, Ratter S, Tomlin S, Williams J, Dacie JE, Rees LH, Besser GM
Dept. Endocrinology, St. Bartholomew's Hosp., London EC1A 7BE, England
Br Med J; 284(6308):9-12 1982

Twenty-three patients with ACTH-dependent Cushing's syndrome were subjected to selective venous catheterization and sampling for ACTH on a total of 26 occasions. Out of 10 patients with pituitary-dependent disease, 9 had raised ACTH concentrations in one or both high internal jugular vein samples. Eight patients had 11 proved sites of ectopic hormone production: of these, 6 were correctly identified by the sampling technique, and in 4 of them this was the only accurate method of localization. The results of one catheterization were misleading, and on 10 occasions they were inconclusive; five patients remained undiagnosed by any method. Overall, 15 of the 26 catheterizations provided diagnostically valuable information. Selective venous catheterization and sampling for ACTH is effective in confirming a pituitary source of the hormone and may be valuable in locating the source of ectopic ACTH production in some cases. (Author abstract) (21 Refs)

6. MULTIPLE FORMS OF IMMUNOREACTIVE BETA-ENDORPHIN ARE PRESENT IN AN ECTOPIC ADRENOCORTICOTROPIN-PRODUCING TUMOR BUT NOT IN NORMAL PITUITARY OR PITUITARY ADENOMAS.

Suda T, Tozawa F, Yamaguchi H, Shibasaki T, Demura H, Shizume K
Dept. Medicine, Tokyo Women's Medical Coll., 10-Kawada-Cho, Ichigaya, Shinjuku-ku, Tokyo 162, Japan
J Clin Endocrinol Metab; 54(1):167-171 1981

Human ACTH-producing tumor and plasma have been examined by gel filtration and ion exchange chromatography to detect the possible presence of reported multiple forms of immunoreactive beta-endorphin (I-EP). Ion exchange chromatography of I-EP obtained from gel filtration showed four components of I-EP [2 major peaks in the positions of EP-(1-31) and EP-(1-27) and 2 minor peaks in the positions of N-acetyl EP-(1-31) and N-acetyl EP-(1-27)] in two ectopic ACTH-producing lung cancers, and two components of I-EP [the major peak in the position of EP-(1-31) and the minor peak in the position of N-acetyl EP-(1-31)] in an ectopic ACTH-producing thyroid cancer. Only a single peak in the position of EP-(1-31) was present in plasma from a patient with Nelson's syndrome and a patient with Addison's disease, in the pituitary adenomas from six patients with Cushing's disease, and in the nontumorous pituitary tissues from a patient with Cushing's disease and a patients with acromegaly. These data suggest that the posttranslational processing of EP in human pituitary is different from that in the ectopic ACTH-producing tumor. (Author abstract) (12 Refs)

7. LYMPHOCYTIC ADENOHYPOPHYSITIS OF PREGNANCY SIMULATING A PITUITARY ADENOMA: A DISTINCT PATHOLOGICAL ENTITY. REPORT OF TWO CASES.

Baskin DS, Townsend JJ, Wilson CB
(c/o The Editorial Office) Dept. Neurological Surgery, Univ. California Sch. Medicine, 350 Parnassus Ave., Suite 807, San Francisco, CA, 94117
J Neurosurg; 56(1):148-153 1982

Diffuse lymphocytic infiltration of the adenohypophysis occurring in temporal relation to pregnancy was found in two patients, each of whom had an intrasellar mass with suprasellar extension that caused compression of the optic chiasm. The pathology and etiology of this lesion is discussed. This entity should be considered when evaluating patients with a pituitary mass lesion that presents in temporal association to pregnancy, particularly if there is evidence of hypopituitarism rather than a hypersecreting, endocrine-active adenoma. (Author abstract) (27 Refs)

8. TUMOR OF THE PINEAL BODY REGION IN CHILDREN.

Bai G, Luo S, Li D
Dept. of Neurosurgery, Xuanwu Hosp., Beijing, People's Republic of China
Zhonghua Waike Zazhi; 19(4):216-219 1981

Tumors of the pineal body region are relatively rare, representing 1-2% of intracranial tumors reported in the literature. Diagnosis and treatment are described for 48 cases (37 males, 11 females; aged 1.5-15 yr) seen between 1955 and 1978; they represented 4.4% of all intracranial tumors seen during the same period. The most common tumors observed in this series included 24 cases of teratoma (50%), 9 cases of pinealoma, 2 cases of pineal blastoma, and 9 cases of glioma. Major presenting symptoms included intracranial hypertension (100%), disturbance of upper movement of the eyeball (62.5%) and cerebellar signs (25%). The most useful diagnostic technic used was cerebral ventriculography which not only could determine the position of the tumor but also could sometimes determine its nature. Surgery was the treatment o f choice. Different surgical technics are discussed. (7 Refs) (In CHI)

THYROID TUMORS

9. EVALUATION OF HUMAN THYROID TUMORS BY PROTON NUCLEAR MAGNETIC RESONANCE.

de Certaines J, Herry JY, Lancien G, Benoist L, Bernard AM, Le Clech G
Centre Eugene Marquis, C.H.R. de Pontchaillou, Rennes, France
J Nucl Med; 23(1):48-51 1982

Proton nuclear magnetic resonance (NMR) was used in a study of 40 patients with thyroid tumors following partial or total thyroidectomy. Three patient groups were considered: those with nodules showing increased uptake, those with solitary nodules with decreased uptake, and those with multinodular goiters. Spin-lattice and spin-spin relaxation times (T1 and T2) were measured on samples of nodular and extranodular tissue from each patient. Increased T1 and T2 were observed for benign cold nodules, an increase in T1 alone for nodules with increased uptake, and a wide fluctuation in T1 and T2 for multinodular goiters. The four cancers in the series did not show a distinctive proton NMR pattern in comparison with the other nodular structures studied. The results point to the feasibility of applying NMR techniques to the detection of thyroid disease. (Author abstract) (4 Refs)

10. EARLY DIAGNOSIS OF THYROID CANCER.

Demidov VP, Gol'bert ZV, Voronetskii IB, Sergeev SA, Ageev IS
Dept. Head and Neck Tumors, P. A. Hertsen Res. Oncological Inst., Moscow, USSR
Sov Med; (10):101-103 1981

Diagnostic efficacy of complex examination was evaluated in 323 patients with nodular thyroid disease. Early thyroid carcinoma was detected in 93/363 patients (69/224 with adenomas, 19/79 with chronic nonspecific thyroiditis, and 5/20 with nodular goiter). Clinical symptoms of early cancer included prolonged history of a nodule (greater than 1 yr), rapid growth of the nodule during the last 6 mo, solid structure, and the presence of multiple nodules. Correct clinical diagnosis of thyroid cancer was made only in 22.6% of the patients. Scintigraphy with 131I showed 'cold' nodules in 37.6% of the patients with early cancer and in 27.1% of the patients with dysplasia. Correct cytological diagnosis of early cancer was made in 52.3% of the patients. At lymphography, irregular contour of the filling defect was observed in 95.8% of the patients with early cancer. Lymphography visualized cancer nodules up to 0.3 cm in diameter. (9 Refs) (In RUS)

11. FINE-NEEDLE ASPIRATION CYTOLOGY IN THYROID DISEASE.

Willems JS, Lowhagen T
Div. Cytology, Dept. Tumour Pathology, Karolinska Hosp., S-104 01 Stockholm, Sweden
Clin Endocrinol Metab; 10(2):247-266 1981

The find-needle aspiration biopsy technique (also called aspiration biopsy cytology or ABC) is described in detail, and the cytological patterns of thyroid disorders that can be diagnosed are described. Needles of 0.6-0.7 mm external diameter are used. Sampling is done with a 10-20 ml disposable plastic syringe held in a 'one-hand' syringe holder. Air drying and staining of the aspirate with May-Grunwald-Giemsa (MGG) provides the best preparation for observing cytoplasmic details and extracellular substances with light microscopy. Most thyroid gland disorders are recognizable with ABC. Characteristic cytological appearance of cogenital abnormalities, inflammatory conditions (acute suppurative thyroiditis), subacute/granulomatous (de Quervain or giant cell) thyroiditis, chronic lymphocytic thyroiditis (Hashimoto's struma), fibrous thyroiditis (Riedel's struma), and hyperplasia (non-toxic, or simple colloid, goiter, toxic goiter) are described with illustration of their microscopic appearance. Characteristic cellular appearances of aspirates associated with follicular adenomas, follicular carcinomas, papillary neoplasms, medullary carcinoma, anaplastic carcinoma, and lymphoma are described, with photomicrographs of air-dried, MGG-stained smears. Recent clinical experience shows that false positive diagnoses using ABC are rare (none reported since 1970), but false negatives have ranged from 6.6 to 27.5% in six different studies. (16 Refs)

12. NEEDLE BIOPSY PATHOLOGY.

Vickery AL
Harvard Medical Sch., Boston, MA, 02115
Clin Endocrinol Metab; 10(2):275-292 1981

Experience from application of the large-needle biopsy technique to 1,981 patients at Massachusetts General Hospital is reviewed, with comments on clinical experience and on the r
ed literature. Hashimoto's thyroiditis, subacute thyroiditis,
del's thyroiditis, follicular adenomas, atypical hyperplasia,
bryonal (trabecular) and fetal (microfollicular) adeno
cystic lesions, and malignant tumors (papillary carcinoma, f
cular carcinoma, medullary carcinoma, undifferentiated ca
noma, metastatic carcinoma, malignant lymphoma, Hur
cells) are discussed, and photomicrographs of biopsy specim
are presented for several of the diseases. False positive res
were obtained in 5/73 patients; false negatives ranged from
14% of those tested. (16 Refs)

13. PATHOLOGY OF THE COLD NODULE.

Brown CL
London Hosp. Medical Coll., London E1, England
Clin Endocrinol Metab; 10(2):235-245 1981

Pathological characteristics of thyroid nodules that fail
bind radioiodide or pertechnetate (cold nodules) are reviewe
Gross and microscopical appearance of colloid nodules, cys
and adenomas are described. Histological identifying characte
istics of unmetastasized differentiated thyroid carcinomas a
given, with photomicrographs. Limitations of several metho
which have been suggested as substitutes to conventional th
roid-seeking isotopic scanning are indicated. Operative biops
continues to be the preferred diagnostic treatment in all cas
of solitary cold nodule of the thyroid. (27 Refs)

14. ELECTRON MICROSCOPIC STUDY ON MITOCHONDRIA IN HURTHLE CELL ADENOMA OF THYROID.

Satoh M, Yagawa K
Dept. Oral Pathology, Sch. Dentistry, Iwate Medical Univ., 19-1 Uchimaru, Morioka, Japan
Acta Pathol Jpn; 31(6):1079-1087 1981

In this investigation Hurthle cell adenoma of the thyroid was observed by electron microscpy. The cytoplasm of the cells consisted chiefly of an accumulation of numerous irregularly shaped mitochondria. Very few other organellae were observed. In addition electron microscopy revealed various degrees of electron density in the matrix of the mitochondria. When three dimensional models of the mitochondria were constructed, they revealed the mitochondria to have three dimensional forms which sometimes looked as if they might be dividing into two or three parts. The authors felt that this indicted a process of vigorous division of mitochondria and an extension of their life span. However, it was not possible to identify the cause of this division of mitochondria. (Author abstract) (23 Refs)

15. TREATMENT OF WELL-DIFFERENTIATED THYROID CARCINOMA.

Block MA
Dept. Surgery, Scripps Clinic and Res. Foundation, 10666 North Torrey Pines Road, La Jolla, CA, 92037
Compr Ther; 7(12):52-58 1981

Recognition, clinicopathologic features, and management of well-differentiated thyroid carcinoma are reviewed. The tumor is often occult. Appearance of a palpable and sometimes visible nodule of the thyroid gland provides the initial clue to thyroid carcinoma. Occasionally an enlarged lymph node in the lateral cervical region is the first overt evidence of pathology and indicates metastasis. The use of diagnostic needle biopsy has improved identification of thyroid nodules and has permitted definitive treatment. Diagnostic needle biopsy has allowed greater definition of nodules that require surgery: the incidence of carcinoma at resection may reach as high as 86%. Since the biologic aggressiveness of thyroid carcinoma is different in each patient, basic characteristics for each category of disease must be recognized to adapt surgery to the individual patient. Characteristics of papillary vs follicular carcinoma are discussed. Factors determining extent of surgery, previous external radiation therapy, postoperative care, avoiding technical therapy, results of primary treatment, and treatment of metastases are discussed. (24 Refs)

16. OXYPHIL TUMORS OF THE THYROID: FOLLOW-UP OF 42 SURGICAL CASES.

Bondeson L, Bondeson AG, Ljungberg O, Tibblin S

(c/o A. G. Bondeson) Dept. Surgery, General Hosp., S-214 01 Malmo, Sweden

Ann Surg; 194(6):677-680 1981

Histopathologic and clinical follow-up data on 42 patients observed 2-20 years after operations for oxyphil neoplasms of the thyroid are presented. In eight patients histologic signs of malignancy were found but only two patients showed a clinically malignant course with development of distant metastases. The results do not indicate that oxyphil thyroid neoplasms are especially prone to assume a malignant course with the mode of treatment applied. Our policy is to remove any differentiated epithelial thyroid neoplasm with at least lobectomy. Total thyroidectomy is reserved for cases with capsular penetration, blood vessel invasion and/or metastases. (Author abstract) (10 Refs)

17. THE USE OF RADIOIODINE IN THE MANAGEMENT OF THE DIFFERENTIATED THYROID CANCER.

Bestagno MF, Pagliaini R, Maira G, Terzi A

Nuclear Medicine Dept., City Hosp., Brescia, Italy

J Radioanal Chem; 65(1/2):239-249 1981

Use of radioiodine in management of 270 cases of differentiated thyroid cancer (DTC) is reported. The first and primary step in therapy was total thyroid ablation. As much of the thyroid was removed as possible without damaging nerves or parathyroid glands. Following surgery, 131I was administered (usual dose 80 mCi) to eradicate remaining thyroid tissue. A total body (TB) scan was performed on day 3 or 5 after treatment (AT). Patients with no indication of metastases were reexamined after 6 mo using a 5 mCi tracer dose and, if still without metastases, were put on a follow-up program. Patients with metastases received radioiodine therapy (usual dose 200 mCi, repeated every 3-6 mo) until disappearance of the focus. TB scans were performed after each treatment. Side effects were minimal. Of 202 cases, 119 were free of metastases (FOM), 62 had nodal involvement (LNI), and 21 had bone or lung metastases (BLM). Metastases were found by TB scan in 9.2% of FOM patients, 37.0% of LNI patients, and 28.6% of BNM patients. Patients with metastases detectable only by TB scan had a better prognosis than those with clinical or radiological signs. Results indicate that TB scans are useful for diagnosis and therapy of DTC, and that total thyroid ablation is required for successful detection of metastases. Safety precautions taken in conjunction with diagnosis and treatment are described. (38 Refs)

18. THE MANAGEMENT OF RADIATION-INDUCED TUMOURS OF THE THYROID.

Korff JM, DeGroot LJ

Univ. Chicago Pritzker Sch. Medicine, Univ. Chicago Hosp. and Clinics, Chicago, IL

Clin Endocrinol Metab; 10(2):299-315 1981

Procedures are explained for the management of the thyroid tumors found in patients who have undergone neck irradiation in childhood. Management begins with the physical examination; patients with normal thyroid and no symptoms are advised to submit to re-examination every 2 yr and receive no further treatment. Patients with equivocal results of physical examination or with diffusely enlarged thyroi ds are given 99Tc pinhole-camera scintigraphy; those whose thyroids show diffuse uptake have thyroid tests and appropriate treatment and those whose thyroids exhibit a distinct nodule enter the same management path as those whose thyroids revealed distinct nodules on earlier physical examination. Total extracapsular lobectomy is followed by frozen section biopsy to determine the existence of malignancy. Benign tumors are removed by more or less subtotal thyroidectomy. Differentiated carcinoma and undifferentiated carcinoma both indicate near-total thyroidectomy. Surgery is followed by 131I scan, 131I uptake, chest x-ray, and a measurement of serum thyroglobulin (TG) level as appropriate, for the patients with differentiated carcinoma. Serum TG, bone scan, and chest x-ray are used for those with undifferentiated carcinoma. Depending upon the results of the above tests, treatments are selected from the following: external radiotherapy, injections of 30-50 mCi 131I, chemotherapy, and administration of thyroxine or tri-iodothyronine. (57 Refs)

19. FAMILIAL MEDULLARY THYROID CARCINOMA AND C CELL HYPERPLASIA.

Wolfe HJ, Delellis RA

Dept. Pathology, New England Medical Center, 171 Harrison Ave., Boston, MA, 02111

Clin Endocrinol Metab; 10(2):351-365 1981

Normal C cells are clearly identified by their positive calcitonin test when calcitonin antisera and immunofluorescent or immunoperoxidase techniques are used. Medullary thyroid carcinoma are rich in calcitonin. In a study of the J kindred, including four generations and 83 family members, 12 members had calcitonin levels which could be elevated to greater than 2.0 nanog/ml upon stimulation and had bilateral medullary thyroid carcinoma located in the middle third of the lateral lobes--the site of greatest C cell density in normal glands. None of the patients had exhibited physical abnormalities before total thyroidectomy was undertaken. In a 9-yr study involving the J kindred, annual calcium gluconate infusion or pentagastrin injection used to detect calcitonin secretory reserve yielded a total of 21 patients in the group who converted from normal to abnormal levels. Except for one false negative, all glands resected from these patients showed bilateral C cell abnormalities ranging from hyperplasia to microscopic carcinoma. A hypothesis for familial medullary thyroid carcinoma proposes an increase in number and size of C cells with progression until C cell hyperplasia breaks through the basement membrane of the thyroid interstitium. Calcitonin is an efficient marker for tumor cells and has allowed early detection of carcinomas previously detectable only after metastasis. C cell hyperplasia is thought to be a manifestation of a mutational event that is hereditary; a hypothetical second mutational event leads to neoplasia. All members of a family in which familial disposition to medullary thyroid carcinoma has been established by histopathological detection of C cell hyperplasia should be screened annually for abnormalities of calcitonin secretory response, and for abnormalities of adrenal medullary and parathyroid functioning. Surgery should follow when tests are positive. (46 Refs)

20. THE DIFFERENTIAL DIAGNOSIS OF HYPERCALCITONINISM.

Dambacher MA, Born W, Heitz PU, Olah AJ, Tobler PH, Fischer JA
Forschungslabor fur Calciumstoffwechsel, Orthopadische Universitatsklinik Balgrist, Forchstrasse 340, CH-8008 Zurich, Switzerland
Schweiz Med Wochenschr; 111(49):1897-1901 1981

Plasma levels of calcitonin (CT) are highest in patients with medullary thyroid carcinoma (MTC). Plasma CT is also raised in some patients with carcinoma such as that of the breast, the lung or the pancreas, and in pheochromocytoma. It must be kept in mind, however, that plasma CT can be similarly raised in patients with renal failure, non-tumoral pulmonary disease or acute pancreatitis. In hypercalcemic patients with primary hyperparathyroidism the plasma CT is normal or only marginally elevated. It is speculated that the raised levels in pregnant and lactating women and in new-born infants prevent excessive bone destruction at times of greater physiological need for calcium. Larger mol wt forms than monomeric CT-(1-32) are circulating at least in plasma of patients with calcitonin-producing tumors and in renal insufficiency. The biological function of these larger molecular wt forms is not yet known. The discrepancies among the results of different laboratories can in part be explained by the immunoheterogeneity of the hormone and the different antigenic recognition sites of the antisera used. The measurement of plasma CT levels is nevertheless important for the diagnosis of MTC and may prove useful in some patients with malignant tumors unrelated to the C-cells of the thyroid gland. CT-radioimmunoassay may be improved by using antibodies specific to the different forms of circulating calcitonin. (Author abstract) (16 Refs) (In GER)

21. RADIOIMMUNOASSAY OF THYROGLOBULIN IN HUMAN SERUM: CONCENTRATIONS IN NORMAL SUBJECTS AND IN PATIENTS WITH THYROID DISEASE.

Roti E, Robuschi G, Emanuele R, Bandini P, Gnudi A
Cattedra di Endocrinologia e Patologia Costituzionale, Univ. Parma, Via Gramsci 14, 43100 Parma, Italy
J Nucl Med Allied Sci; 25(3):57-63 1981

A specific radioimmunoassay for detection of thyroglobulin (hTG) in the blood sera of the patients with various thyroid diseases was developed. Mean value of hTG in the blood sera of healthy controls was 18.2 nanog(ng)/ml. Higher than normal concentrations of hTG were detected in patients with toxic Grave's disease (213.9 ng/ml), idiopathic hypothyroidism (46.8 ng/ml), euthyroid goiter (164.6 n g/ml), and in th euthyroid and hyperthyroid states of nodular goiter (164.6 and 168.0 ng/ml, respectively). Concentrations of hTG in the patients with thyroid cancer (before thyroidectomy) ranged from 25 to 2,750 ng/ml. Values in these patients were in part comparable to those of other thyroid patients, hence indicating limited value as a marker in diagnosis of thyroid cancer. (17 Refs)

PARATHYROID TUMORS

22. PARATHYROID SCINTIGRAPHY WITH 131CS AND 201TL.

Ferlin G, Conte N, Borsato N, Perelli R, Fioretti P, Gasparoni P, Camerani M
Servizio di Medicina Nucleare, Ospedale Generale Provinciale, 31033 Castelfranco Veneto, Italy
J Nucl Med Allied Sci; 25(3):119-123 1981

Diagnostic efficacy of scintigraphy with 131-cesium (131Cs) was studied in 11 patients (2 men, 9 women, 31-64 yr old) with hyperparathyroidism. Surgery was performed in seven patients: all were found to have parathyroid adenoma. Among these patients, six had increased 131Cs accumulation. One patient with a 131Cs-negative scan at operation had a small (less than 0.5 cm in diameter) adenoma. Identical results were obtained in three Cs-positive patients in which the test was repeated with 99mTc pertechnetate and 201thallium. (13 Refs)

23. CHARACTERISTIC ULTRASTRUCTURAL FEATURES OF PARATHYROID GLAND CANCER. A REPORT ON 9 CASES.

Monges G, HenryJF, Casanova P, Garbe L, Sudan N, Payan H
(c/o Payan) Laboratoire d'Anatomie Pathologique, Groupe hospitalier de la Timone, chemin de l'Armee d'Afrique, F 13385 Marseille Cedex 5, France
Ann Pathol; 1(4):298-304 1981

The authors have studied nine parathyroid carcinomas under the electron microscope (3% of their parathyroid lesions). Two types of the ultrastructural features were significant: (1) architectural: basal membrane abnormalities, sparse desmosomes, absence of nerve fiber; (2) cytological: nuclei atypism and abnormal mitochondria in tumor cells resembling dark chief cells. Also noticed were signs of cell hyperactivity and/or trouble in parathormone production or regulation. (Author abstract) (18 Refs) (In FRE)

24. PARATHYROID CARCINOMA: A CLINICAL STUDY OF SEVEN CASES OF FUNCTIONING AND TWO CASES OF NONFUNCTIONING PARATHYROID CANCER.

Aldinger KA, Hickey RC, Ibanez ML, Samaan NA
(c/o Samaan) Section Endocrinology, Dept. Medicine, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Cancer; 49(2):388-397 1982

Seven cases of functioning and two cases of nonfunctioning parathyroid carcinoma are presented together with a general discussion of this disease. Functioning parathyroid carcinoma may be associated with prolonged survival. The morbidity and mortality from this disease are generally related to the prolonged hypercalcemia that occurs. The hypercalcemia is best treated with excision of local recurrence s; however, this surgery is most often palliative and seldom curative. The best operative results were obtained when the disease could be localized preoperatively. Neck and mediastinal exploration in the absence of physical or radiographic evidence of recurrence failed to affect serum calcium levels. Two patients with nonfunctioning parathyroid cancer did poorly compared with those with functioning parathyroid carcinoma. The few cases reported in the literature are also suggestive of a more aggressive disease. The failure of this tumor to produce parathyroid hormone may allow it to escape clinical attention until it has achieved an advanced state. (Author abstract) (45 Refs)

25. HUMAN CHORIONIC GONADOTROPIN SUBUNIT MEASUREMENT IN PRIMARY HYPERPARATHYROIDISM.

Stock JL, Weintraub BD, Rosen SW, Aurbach GD, Spiegel AM, Marx SJ
NIH, Building 10, Room 9D20, Bethesda, MD, 20205
J Clin Endocrinol Metab; 54(1):57-63 1982

The concentration of subunits of hCG (hCG alpha and hCG beta) was determined in plasma or serum from 70 patients with primary hyperparathyroidism (1 degree HPT). Two of three patients with parathyroid carcinoma showed elevation in plasma concentrations of both subunits, which fell after surgical removal of the tumor. An extract prepared from the tumor of one of these patients contained the subunits in high concentrations, whereas in extracts similarly prepared from tissues removed from seven patients with benign 1 degree HPT, the subunits were not detectable or were present in much lower concentrations. In 42 cases of benign 1 degree HPT, samples from veins containing a 10-fold gradient of parathyroid hormone obtained during selective venous catheterization and peripheral samples from the same patients were analyzed for hCG subunits. Only one patient demonstrated a mild elevation of hCG alpha in parathyroid venous effluent alone that may have represented subunit release by apparently benign parathyroid tissue. Thirty patients with multiple endocrine neoplasia type I were tested; eight evidenced clinically active islet cell tumors, and six of these eight showed high circulating concentrations of hCG alpha (and hCG beta in one case). Patients in the multiple endocrine neoplasia type I group with 1 degree HPT or pituitary tumors, but no evident pancreatic islet disease, did not show elevations in subunit concentrations. Thus, in patients with 1 degree HPT, determination of subunits of hCG may be helpful in making the diagnosis of parathyroid carcinoma or in screening for associated (and probably malignant) pancreatic islet disease. (Author abstract) (36 Refs)

ADRENAL TUMORS

26. COMPUTED TOMOGRAPHY IN THE LOCALIZATION OF ALDOSTERONE-SECRETING ADRENAL ADENOMAS.

Meek DR, Duncan JG, McAreavey D
Dept. Radiology, Royal Infirmary, Glasgow G4 OSF, Scotland
Br J Radiol; 54(648):1039-1043 1981

Computed tomography (CT) has been shown to detect both adrenal glands in 88.5% of upper abdominal examinations and can visualize at least one gland in 96.5% of patients. However, in examinations carried out specifically to visualize the adrenals, the glands were located in 98% of cases. This technique was used in 18 patients with primary aldosteronism to localize aldosterone-secreting adrenal tumors and to distinguish these from non-adenomas (bilateral adrenal hyperplasia). The results were compared with quadric analysis, a statistical technique used to predict the likely surgical outcome. In seven patients the CT results were verified by operation (6 adenomas, 1 adrenal hypertrophy). However, in one further patient a large adenoma (20 mm in diameter) which had not been predicted by CT scanning was found at operation. In the remaining 10 patients who have been medically treated, results concordant with quadric analysis were obtained in 8 cases. We would suggest that CT scanning should be the initial investigation for the pre-operative localization of adenomas but further comparative studies are required. (Author abstract) (26 Refs)

27. SONOGRAPHY OF ADRENAL PHEOCHROMOCYTOMAS.

Bowerman RA, Silver TM, Jaffe MH, Stuck KJ, Hinerman DL
Dept. Radiology, Div. Ultrasound, Univ. Michigan Medical Sch, Univ. Hosp., Ann Arbor, MI, 48109
AJR; 137(6):1227-1231 1981

The sonographic features of eight surgically confirmed pheochromocytomas are described and correlated with pathologic findings. The purely solid masses were homogeneous or heterogeneous sonographically. Pathologic examination of the gross specimen provided explanations for the variety of sonographic findings. Two tumors had large cystic components due to old blood. Other hypoechoic areas corresponded to necrosis pathologically. Hyperechoic areas represented hemorrhage. Generally, pheochromocytomas are quite large, sharply marginated, and usually have a significant solid component with or without central necrosis or hemorrhage. Recognition of these features should facilitate their identification on sonography. (Author abstract) (27 Refs)

28. POSITIVE DIAGNOSIS AND ANATOMIC LOCATION OF PHEOCHROMOCYTOMAS. THIRTY-THREE CASES IN LESS THAN 5 YR.

Duclos JM, Plouin PF, Brisset JM, Menard J
Service d'Urologie, Hopital Saint-Joseph, 7, rue Pierre Larousse, 75674 Paris, France
Ann Urol (Paris); 15(6):403-405 1981

Most of the 33 pheochromocytoma patients (17-72 yr old) of this study were referred because of hypertension. Patients who presented with headaches, sweating, and palpitations were subjected to biochemical tests for urinary excretion of vanillylmandelic acid (VMA), metanephrines (ME), and/or catecholamines (CCL). If 2/3 of these metabolites were elevated, a positive diagnosis was made. In 28 patients who underwent all tests, a positive diagnosis led to surgical intervention. Tests for VMA and CCL yielded four false negatives. Supplementary examinations included a series of thoracic radiographs and iv urography (which permitted exploration of the kidney as a tumor site). Arteriography was performed but was found to be unsatisfactory because of danger to patients and because of false negatives (5/19). Computed tomography (CT) was used only to confirm a diagnosis which was not changed because of a negative result of the CT examination. (4 Refs) (In FRE)

29. ACCURACY OF ANGIOGRAPHY IN THE LOCALIZATION OF PHEOCHROMOCYTOMA.

Kadir S, Robinette C
Russel H. Morgan Dept. Radiology and Radiological Sciences, Johns Hopkins Medical Inst., Baltimore, MD, 21205
J Urol; 126(6):789-793 1981

An analysis of 20 patients who underwent angiographic localization of pheochromocytoma is presented. The tumors were localized accurately by arteriography in all 20 patients, by excretory urography in 4 of 13 and by computerized body tomography in 3 of 5. Venous sampling and venography were invaluable aids in the localization of pheochromocytomas in patients with postoperatively elevated catecholamine levels, or in the evaluation of recurrence or metastases. The tumors were extra-adrenal in 7 patients, bilateral in 4 and malignant in 5. The majority of these tumors occurred in women. (Author abstract) (18 Refs)

30. SIMPLE SCREENING PROCEDURE FOR THE DIAGNOSIS OF PRIMARY ALDOSTERONISM.

Lund JO, Nielsen MD, Giese J

Dept. Clinical Physiology, Frederiksberg Hosp., DK-2000 Copenhagen F, Denmark

Acta Med Scand; 210(5):393-396 1981

A simple screening protocol for the diagnosis of primary aldosteronism was applied to 149 hypertensive patients. The diagnostic criterion for possible primary aldosteronism was the combination of supine plasma renin concentration less than 15 mIU/l (normal range 6-54) and plasma aldosterone concentration greater than 11 ng/100 ml (normal range 3-18). None of 63 persistently normokalemic hypertensive patients fulfilled this criterion. Seventeen (20%) of 86 hypokalemic patients showed hormonal values consistent with primary aldosteronism. The presence of an adrenal adenoma was verified in eight of these patients. Thus screening for primary aldosteronism can be restricted to hypokalemic patients. The prevalence of primary aldosteronism in a hypertensive population was calculated to be less than 1%. (Author abstract) (20 Refs)

PANCREAS TUMORS

31. ENDOCRINE-PARACRINE CELLS IN PANCREATIC EXOCRINE CARCINOMAS.

Eusebi V, Capella C, Bondi A, Sessa F, Vezzadini P, Mancini AM

Istituto de Anatomia e Istologia Patologica, Policlinico S. Orsola, Via Massarenti 9, Bologna, Italy

Histopathology; 5(6):599-613 1981

Eleven cases of pancreatic adenocarcinoma (PA) were studied with light and electron microscopy and immunoperoxidase staining to characterize the endocrine component of PA. Tissue specimens were taken from a 65-yr-old man during surgery for PA and liver metastasis. Pancreatic and liver tumors showed similar features, with sheets of anastomosing cords of polygonal carcinoma cells fusing with irregular glandular areas. With anti-somatostatin antisera, scattered immunoreactive (IR) cells were indiscriminately detected among non-positive cells. Electron microscopic examination distinguished five different cell types: pure mucinous cells, serotonin-enterochromaffin cells, D-cells, mixed exocrine-endocrine-like cells, and undifferentiated cell types. The other 10 cases of PA were classified as well-differentiated ductal carcinoma (6 cases), poorly differentiated ductal carcinoma (1), acinic cell tumor (1), undifferentiated carcinoma (1), and squamous cell carcinoma (1). Using anti-insulin sera, samples from two cases were shown to contain positive cells. Only one case contained a few scattered glucagon-immunoreactive cells and no cells stained with anti-gastrin, anti-bovine pancreatic peptide, or anti-somatostatin antisera. Seven cases synthesized Alcian blue-positive mucosubstances; five of these also contained argyrophilic cells; no argentaffin elements could be seen. The number of positive cells varied from 5 to 10%. Cells were mostly scattered singly in the glands, wedged between adjacent non-argyrophil columnar cells, but they were also found in the solid tumor cords. (22 Refs)

32. PERCUTANEOUS TRANSHEPATIC PORTAL VEIN CATHETERIZATION IN THE DIAGNOSIS OF HORMONE-PRODUCING TUMORS IN THE SPLANCHNIC AREA.

Luska G, Zick R, Otten G, Mitzkat HJ

Zentrum Radiologie, Arbeitsbereich Krankenhaus Oststadt, Podbielskistrasse 380, D-3000 Hannover 51, W. Germany

ROEFO; 135(5):566-571 1981

During 1980, percutaneous transhepatic portal vein catheterization was carried out in eight patients with suspected hormone-producing tumors in an attempt to localize these. Seven patients with hyperinsulinism were suspected of having an insulinoma and one a gastrinoma. There were no complications following the catheterization, and difficulties were reduced by the use of a special catheter. The blood samples were examined by radio-immunological methods for insulin or gastrin. On the basis of localized rise in hormone level, it was possible to diagnose three insulinomas and one gastrinoma in the pancreas. The beta-cell tumors were removed by enucleation or segmental resection, the gastrinoma by a Whipple's operation. Three patients showed an insulin gradient and sub-total pancreatectomies were performed. In one patient there was no definite abnormality in the insulin level and an operation has so far not been performed. Our experience indicates that this technique is difficult, but is nevertheless a reliable method for localizing hormone-producing tumors and surgery should not be carried out without it. (Author abstract) (31 Refs) (In GER)

33. A MULTIHORMONAL TUMOR OF THE PANCREAS PRODUCING NEUROTENSIN.

Feurle GE, Helmstaedter V, Tischbirek K, Carraway R, Forssmann WG, Grube D, Roher HD

Medizinische Poliklinik, Univ. Heidelberg, Hospitalstrasse 3, 6900 Heidelberg, W. Germany

Dig Dis Sci; 26(12):1125-1133 1981

In a pancreatic adenoma approximately 78.7% of the endocrine cells reacted specifically with antisera to neurotensin, 17.5% to gastrin, 2.8% to pancreatic polypeptide, and 1% to glucagon. The electron microscope revealed that the majority of the endocrine cells were N-cells -- morphologically similar to the ileal N-cells which are known to represent the neurotensin-producing cells. Neurotensin was extracted from the tumor and identified by Sephadex, ion-exchange, and high-pressure liquid chromatography. Gastrin, pancreatic polypeptide, and glucagon cells were also identified by the electron microscope; the peptides were extracted and demonstrated by chromatography. The serum concentrations of these hormones were elevated. After total gastrectomy which was necessary because of Zollinger-Ellison syndrome, a jejunoesophageal alkaline reflux, reaching the upper esophagus appeared. As intravenous infusion of synthetic neurotensin in rats caused an increase of luminal enteric pressure, it is suggested that severe jejunoesophageal reflux after gastrectomy may be a clinical feature of a neurotensinoma. (Author abstract) (24 Refs)

GONADAL TUMORS

34. NEUROHORMONAL PEPTIDES IN OVARIAN CARCINOIDS: AN IMMUNOHISTOCHEMICAL STUDY OF 81 PRIMARY CARCINOIDS AND OF INTRAOVARIAN METASTASES FROM SIX MID-GUT CARCINOIDS.

Sporrong B, Falkmer S, Robboy SJ, Alumets J, Hakanson R, Ljungberg O, Sundler F
Dept. Obstetrics and Gynecology, Malmo General Hosp., S-214 01 Malmo, Sweden
Cancer; 49(1):68-74 1982

Eighty-one primary ovarian carcinoids and intraovarian metastases from six mid-gut carcinoids were examined for the presence of tumor cells immunoreactive with antisera raised against various neurohormonal peptides, mostly of gastroenteropancreatic (GEP) origin. Twenty of the primary and two of the metastastic carcinoids contained such tumor cells. The incidence of tumors with any kind of neurohormonal peptide immunoreactive tumor cells was 53% in the trabecular carcinoids, and 42% in the strumal carcinoids, whereas the incidence was much lower (7%) in the insular type. Immunoreactive pancreatic polypeptide (PP), glucagon, enkephalin, and somatostatin were those neurohormonal peptides most commonly observed in the tumor cells of the primary carcinoids. Those less commonly found were substance P, calcitonin, VIP, neurotensin, beta-endorphin, and ACTH. Four metastatic carcinoids were nonreactive with all the antisera used. Cells storing immunoreactive insulin, glucagon, PP, VIP, gastrin, substance P, or enkephalin were found in one of the two remaining metastatic carcinoids; in the other only gastrin-immunoreactive tumor cells were observed. The occurrence and distribution of tumor cells storing the neurohormonal peptides in ovarian carcinoids are discussed in relation to their possible origin in the ovary and to carcinoids in the gut. (Author abstract) (32 Refs)

35. ON MALIGNANCY OF HORMONE-PRODUCING TUMORS OF THE OVARY.

Kozachenko VP, Adamian RT, Pitchugina MW, Filatova AM
Center Oncology Res., USSR Acad. Medical Sciences, Moscow, USSR
Vopr Onkol; 27(10):40-44 1981

Four hundred and one cases of hormone-producing tumors of the ovary were studied (190 theca-cell, 169-granulosa cell, 25 mixed theca-granulosa cell and 17 virilizing tumors). Histological diagnosis, clinical stage and end results of their treatment were compared. Theca-granulosa cell tumor is considered to be the most malignant form of these neoplasms. Pure theca-cell tumor proved to be benign in most cases. Of special interest is a high percentage of patients being cured at Stage 1 (FIGO classification) of neoplastic process, that stands, in the authors' opinion, in close relationship with comparatively good results obtained in these patients. (Author abstract) (11 Refs) (In RUS)

36. BIOLOGICAL MARKERS FOR TUMORS OF THE TESTIS: THEIR USE IN DIAGNOSIS PROGNOSIS AND FOLLOW-UP IN 200 CASES.

Bellet D, Caillaud JM, Droz JP, Delarue JC, Bohuon C
Service de Biologie Clinique, Inst. Gustave Roussy, F 94800 Villejuif, France
Nouv Presse Med; 10(40):3293-3297 1981

Repeated measurements of serum chorionic gonadotrophic hormone (CGH) of its beta sub-unit (beta-CGH) and of alphafetoprotein (aFP) were performed in 200 patients with germinal tumors of the testis. CGH levels were found to be high in 43.5% of patients, particularly those with choriocarcinoma (a rare tumor) or with embryonal carcinoma with syncytiotrophoblastic (ST) cells. They were also high in 24% of patients with histologically pure seminoma, which throws doubts on the homogeneity of this group of tumors and raises problems concerning their treatment in patients with high CGH. aFP levels were increased in 38% of all patients, particularly those with ST cell embryonal carcinoma (62%) or with malignant teratoma (56%). These biochemical markers may point to a histological diagnosis. They also have prognostic value and are essential for monitoring during treatment. Pre-operative assays are of particular interest and should be performed in every case. (Author abstract) (22 Refs) (In FRE)

OTHER TUMORS OF GLANDULAR TISSUES

37. HORMONAL RECEPTORS AND RESPONSE TO TREATMENT OF BREAST CANCER: A RETROSPECTIVE EVALUATION IN 60 PATIENTS.

Loven D, Rakowsky E, Stein JA, Geier A, Lunenfeld B
Inst. Oncology, Beilinson Medical Center, 49100 Petah Tikva, Israel
Isr J Med Sci; 17(9/10):960-964 1981

Response to several types of endocrine therapy or chemotherapy was evaluated in 60 patients with breast cancer. Estrogen and progesterone receptors were determined by radioimmunoassay. Response to endocrine therapy was significantly higher (p less than 0.01) among estrogen receptor (ER)-positive cases than among ER-negative cases. The response to chemotherapy did not differ significantly between the two groups. The results of this small series support the conclusion that determination of ER is valuable in planning endocrine treatment of the breast cancer patient, whereas response to chemotherapy does not correlate with ER levels. (Author abstract) (15 Refs)

38. QUANTITATIVE OESTRADIOL RECEPTOR VALUES IN PRIMARY BREAST CANCER AND RESPONSE OF METASTASES TO ENDOCRINE THERAPY.

Campbell FC, Blamey RW, Elston CW, Morris AH, Nicholson RI, Griffiths K, Haybittle JL
(c/o Blamey), City Hospital, Nottingham, England
Lancet; 2(8259):1317-1319 1981

The relationship between estrogen receptor (ER) status of primary breast cancer and response of the secondary cancer to endocrine therapy, and the relationship between response and measured receptor values in the primary tumor were investigated. Six hundred and twenty primary breast cancer patients with tumors less than 5 cm in diameter and no evidence of distant metastasis were treated with simple or sc mastectomy. Endocrine therapy (oophorectomy for premenopausal patients and 20 mg tamoxifen bid for postmenopausal patients) was subsequently administered to 106 patients with evidence of metastasis. Of 95 assessable patients, 19 responded to treatment; 17 of these had ER positive and 2 had ER negative cancer. Median duration of remission was 26 mo for patients with ER receptor-high cancer (greater than 50 femtomole/mg cytosol) and 12.2 mo for those with receptor-low cancer (less than 50 femtomole/mg cytosol). Metastatic tumor biopsy in 24 patients showed unchanged ER status in 18; 3 who had had ER positive primaries developed ER negative secondaries and 3 who had had ER negative primaries had measurable amounts in the secondary tumor. Likelihood and possibly duration of remission of subsequent metastasis after endocrine therapy may be predicted on the basis of the ER value in the primary malignancy at the time of mastectomy. (8 Refs)

39. BREAST CANCER: A COMPARISON OF RESPONSE TO ENDOCRINE THERAPY AND OESTROGEN EXCRETION PATTERNS INCLUDING UNUSUAL METABOLITES.

Castagnetta L, D'Agostino G, Lo Casto M, Traina A, Leake RE
Cancer Hosp. Centre 'Maurizio Ascoli', 90127 Palermo, Italy
Br J Cancer; 44(5):670-674 1981

The urinary excretion patterns of estrogen metabolites, including unusual metabolites, were determined by gas chromatography and mass spectrometry for 63 women with advanced breast cancer and 39 normal postmenopausal women. The concentration of total unusual metabolites excreted was found to be an excellent discriminant between breast-cancer patients and controls (p less than 0.0001). Discrimination between responders and non-responders to endocrine therapy was attempted, using several different indices. Of these, the ratio of Classical Estrogens to Unusual Metabolites (CE/UM) proved a fair discriminant, but the product of this ratio and the estriol ratio (CE/UM x E3R) was much the best discriminant. This product, termed a Pattern Index, has considerable potential, not only as a discriminant for selecting therapy, but also as a rapid index of patient response to that therapy. (Author abstract) (23 Refs)

40. CLINICAL STUDY OF ESTROGEN RECEPTOR IN CHINESE PATIENTS WITH BREAST CANCER.

Liu TJ, Chi CW, Cheng EC, Chyr R, Lee C, P'Eng FK
Div. General Surgery, Dept. Surgery, Veterans General Hosp., Taipei, Republic of China (Taiwan)
Taiwan I Hsueh Hui Tsa Chih; 80(9):909-918 1981

Preliminary studies of the correlation between tumor estrogen receptor (ER) contents and clinical response to endocrine manipulation of 126 recurrent or metastatic breast cancer patients and use of primary cancer specimens to predict hormone dependency of potential metastases are described. Positive ER levels were found in 16/43 Stage I specimens, 11/37 Stage II, 12/16 Stage II, and 7/10 Stage IV. Of the 106 primary and 20 secondary cancer patients, 46 and 5, respectively, were ER+. In the secondary cancer group, 4/16 locally recurrent or chest wall specimens, 1/2 lung and pleural cavity specimens, and 0/2 of cervical lymph nodes from patients with advanced metastatic breast cancer were ER positive. The mean of positive ER was higher in the postmenopausal group (62.85 +-13.91 vs 38.28 +-8.12 femtomole/mg cytosol protein). The same pattern was found in negative ER cases (2.77 +-0.50 vs 1.86 +-0.52 femtomole/mg cytosol protein). Both male breast cancer specimens were ER+. Of 30 benign breast cancer specimens examined, 6 were ER+. Hormonal treatment of 26 patients produced a fairly high response rate in ER+ patients. Ablative therapy was performed in 12 patients (6 ER+ and 6 ER-). All 5/5 ER+ and 0/5 ER- patients responded to oophorectomy. Neither ER+ nor ER- patients responded to bilateral adrenalectomy. Tamoxifen treatment produced responses in 3/5 ER+ and 0/2 ER- patients. Combined therapy with oophorectomy and tamoxifen also produced a good response in two ER+ patients. One ER+ and 1/2 ER- patients responded to oophorectomy and testosterone treatment. Therapy complications are described. Results indicated that the cytoplasmic ER assay in breast cancer patients is a reliable indicator for selection of good responders to hormonal treatment. (25 Refs)

41. MOLECULAR BASIS OF STEROID HORMONE ACTION IN BREAST CANCER AND ITS CLINICAL IMPLICATIONS.

Lunenfeld B, Geier A

Inst. Endocrinology, Chaim Sheba Medical Center, 52103 Tel-Hashomer, Israel

Isr J Med Sci; 17(9/10):954-959 1981

The measurement of steroid hormone receptors in tumors from patients with breast cancer is now established. Data have accumulated that seem to indicate that breast cancer patients may be selected for endocrine or adjuvant therapy on the basis of the presence or absence of estrogen receptors. Furthermore, patients without detectable estrogen receptors seem to have a greater likelihood of early recurrence following mastectomy. We describe recent findings on the mechanism of action of both estrogens and antiestrogens at the normal target cell level. Evidence for a similar mechanism of action for estrogens and antiestrogens in the hormone-responsive mammary tumor cell is presented on the basis of studies in hormone-dependent, dimethylbenz(a)anthracene-induced mammary carcinoma in the rat, and the cell line MCF-7 derived from a human breast carcinoma. The interaction of estrogens and antiestrogens with their receptors in the cytoplasm and nucleus in solid human breast tumors is discussed and analyzed in terms of the potential clinical application to breast cancer management. (Author abstract) (54 Refs)

42. ESTROGEN RECEPTOR CYTOCHEMISTRY IN HUMAN BREAST CANCER: STATUS AND PROSPECTS.

Nenci I

Istituto Anatomia Patologica, Universita di Ferrara, Ferrara 44100, Italy

Cancer; 48(12):2674-2686 1981

Advances in knowledge of the endocrine control of neoplastic growth can be expected to stem directly from advances in pertinent techniques. Following this theme, the present paper describes how recent development in cytochemical techniques for estrogen receptors may maintain this expectation and lead to significant progress in the basic knowledge of breast cancer that can influence the treatment approach. Cytochemical techniques have shown that the binding of estrogen to target cells and tissues can be specifically visualized: moreover, estrogen binding sites characterized cytochemically under controlled conditions have proved to fulfill the accepted criteria for estrogen receptors. Some working solutions to basic questions concerning the tumor hormone-responsiveness have been provided and more precise explanations of fundamental growth-regulatory mechanisms are expected to emerge from the approach to breast cancer by cytologic endocrinology. However, in the present state of the art and in spite of tantalizing bits of data, cytochemical techniques for estrogen receptors do not seem extensible to routine purposes, as alternative to biochemical receptor assays in selecting patients for endocrine therapy. One must have strong reservations on their clinical use because of the almost complete lack of information about correlations of cytochemical results with the response to endocrine therapy. More studies evaluating the practical validity of estrogen receptor cytochemistry are required. (Author abstract) (92 Refs)

43. HOW EFFECTIVE IS SURGICAL ADRENALECTOMY IN LOWERING STEROID HORMONE CONCENTRATIONS?

Worgul TJ, Santen RJ, Samojlik E, Wells SA
(c/o Santen) Dept. Internal Medicine, Div. Endocrinology, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
J Clin Endocrinol Metab; 54(1):22-26 1981

Surgical adrenalectomy produces objective tumor regression in 50-60% of estrogen receptor-positive women with metastatic breast carcinoma. Additional responses to antiestrogens or further suppression of estrogens with aminoglutethimide after adrenalectomy suggest the possibility of continued adrenal steroid secretion even after surgical ablation. The use of sensitive and specific RIAs allows precise determination of the degree of hormone suppression after adrenalectomy and could provide documentation of nonsuppression or escape from suppression in individual patients. To evaluate the possibility of continued hormone secretion, we measured 14 hormones in 26 postmenopausal women with breast carcinoma before and after adrenalectomy. While the mean levels of androgens were markedly suppressed after adrenalectomy, estrogen concentrations fell to a much lesser extent. Examination of data in individual patients revealed incomplete suppression in several women. Androgen concentrations also fell incompletely after adrenalectomy in a few patients. Androstenedione concentrations were greater than 2 SD above the group mean in 2 of 23 patients, and in 2 of 25 patients, DHEA-S concentrations were also greater than 2 SD above the group mean. Serial measurements of hormones over a 1-to 3-yr period following surgery revealed escape from suppression over time in 7 of 26 women. The practical significance of the lack of suppression or of escape from inhibition was assessed by comparing estrogen levels in respondes vs nonresponders to surgical adrenalectomy. Of all steroids measured, greater suppression of only one hormone was observed in responders vs. nonresponders. These data indicate that adrenalectomy does not uniformly suppress circulating androgen and estrogen levels in postmenopausal patients. Women who initially suppress after adrenalectomy may show recovery of either androgen or estrogen levels with time. (24 Refs)

44. STUDIES ON ADRENAL ANDROGEN IN PATIENTS WITH PROSTATIC CARCINOMA RECEIVING ENDOCRINE THERAPY.

Iwasaki A
Dept. Urology, Yokohama City Univ. Sch. Medicine, Yokohama, Japan
Nippon Hinyokika Gakkai Zasshi; 72(6):701-716 1981

Plasma 4-androstenedione (4-A) was measured in 29 normal subjects (10 men 24-27 yr old, 10 women 23-26 yr old, 9 men 60-67 yr old), in 21 patients with prostatic hypertrophy, in 9 untreated patients with prostatic cancer, and in 51 patients treated with hormone therapy for prostatic cancer. Effects of adrenal androgens on reactivation of prostatic carcinoma were studied with 4-A as a marker. Av 4-A levels were 81 +-38 nanog (ng)/deciliter (dl) in the 10 normal men, 105 +-22 ng/dl in the 10 normal women, and 73 +-28 ng/dl in the 9 aged men. No significant differences were observed between 4-A levels at 9 am and at 5 pm, but the 9 am levels were higher. Compared to the aged men, 4-A levels were not significantly different in the patients with prostatic hypertrophy and in those with prostatic cancer. Plasma 4-A, testosterone, and cortisol, concentrations of intratesticular testosterone, and steroidogenesis in resected testicular tissue were studied in 94 patients treated for 2 mo to 9 yr with Hexestrol (HE; 30 mg/day) or chlormadinone acetate (CMA; 100 mg/day). Plasma levels of cortisol were markedly increased due to estrogen therapy. Steroidogenesis was completely blocked in testicular tissue after administration of HE for 2 mo, an intratesticular testosterone concentrations were markedly decreased after administration of CMA for 2 mo. 4-A levels were av 52.9 +-20.0 ng/dl in patients treated for 9 yr with HE and were av 49.9 +-20.9 ng/dl in patients treated with CMA. Reactivation of prostatic cancer due to adrenal androgens was thought to be unlikely. (50 Refs) (In JPN)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

45. EFFECTS OF POSTOPERATIVE ADJUVANT CHEMOTHERAPY AND RADIOTHERAPY ON OVARIAN FUNCTION IN WOMEN UNDERGOING TREATMENT FOR SOFT TISSUE SARCOMA.

Shamberger RC, Sherins RJ, Ziegler JL, Glatstein E, Rosenberg SA
(c/o Rosenberg) Surgery Branch, Div. Cancer Treatment, NCI, NIH, Public Health Service, U.S. Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(6):1213-1218 1981

Ovarian function was evaluated in 11 women 16 to 43 yr of age at treatment who received doxorubicin, cyclophosphamide, and high doses of methotrexate with or without radiotherapy in adjuvant therapy of soft tissue sarcoma. Five women (16-33 yr old) who received chemotherapy alone or combined with radiotherapy only at sites distant from the ovaries (chest wall, thigh, and leg) had minimal menstrual irregularities or temporary cessation of menses during therapy; cyclic menses returned promptly after therapy. Gonadotropin levels (expressed as means +- SD) [follicle-stimulating hormone (FSH), 10 +-5 mIU/ml; luteinizing hormone (LH), 10 +-4 mIU/ml] and 17beta-estradiol (E2) levels (means +- SD, 208 +-147 pg/ml) were normal. By contrast, four older women (ages 36-43 yr) who received similar treatment developed persistent amenorrhea with postmenopausal levels of gonadotropin (FSH, 108 +-29 mIU/ml; LH, 72 +-19 ml U/ml) and E2 (19 +-8 pg/ml). Two additional women (ages 21 and 39 yr) who received radiation (7,000 rad) to the pelvis plus chemotherapy developed prompt cessation of menses and became functional castrates (FSH, 77 and 80 mIU/ml; LH, 40 and 58 mIU/ml; E2, 10 and 19 pg/ml). However, this result would be expected from the radiation dose alone. The data demonstrated that ovarian dysfunction may follow the use of doxorubicin, cyclophosphamide, and high doses of methotrexate and that the injury is age related. (Author abstract) (35 Refs)

46. VERNER-MORRISON SYNDROME.

Fahrenkrug J, Pedersen JH, Schaffalitzky de Muckadell OB, Stadil F
Klinisk kemisk afdeling, Kobenhavns amts sygehus i Glostrup, DK-2600 Glostrup, Denmark
Ugeskr Laeger; 143(44):2881-2885 1981

The first case in Denmark of Verner-Morrison syndrome (VMS) in a 74-yr-old woman is reported, and the literature on VMS is reviewed. The syndrome was caused by a pancreatic tumor. Severe chronic diarrhea, hypokalemia and reduced gastric acid secretion were the cardinal symptoms. The vasoactive intestinal peptide (VIP) level in the serum, determined by radioimmunoassay, was increased significantly and correlated with the intensity of the disease. The tumor was detected by ultrasonic scanning and abdominal arteriography. Hypervascularized hepatic metastases were confirmed by biopsy. Long-term remission, cessation of diarrhea, and reduction of the VIP level to below 80 picomoles/liter were achieved by streptozotocin treatment, embolization of the hepatic artery, and interstitial irradiation. Recurrences were accompanied by rises in the VIP level. The review of the literature on VMS shows that VMS is frequently due to pancreatic VIP-secreting tumor, exclusively in adults, while neurogenic tumors (ganglioneuroma, neuroblastoma, ganglioneuroblastoma, pheochromocytoma, and neurofibroma) occur at all ages, most frequent in children. (30 Refs) (In DAN)

47. RESULTS OF SURGICAL MANAGEMENT IN 92 CONSECUTIVE PATIENTS WITH ZOLLINGER-ELLISON SYNDROME.

Bonfils S, Landor JH, Mignon M, Hervoir P
Unite de Recherches de Gastroenterologie (U.10), Hopital Bichat, 170 Boulevard Ney, 75877 Paris Cedex 18, France
Ann Surg; 194(6):692-697 1981

Hospital records and follow-up information on 92 patients with surgically proven Zollinger-Ellison syndrome have been reviewed, and data relating to symptomatology, age and sex incidence, pathologic findings, and early and late results of surgical procedures have been summarized. The postoperative mortality rate was 15%, and was adversely affected by previous peptic ulcer surgery, by the necessity of urgent operation for complications of peptic ulcer, and by employment of a procedure that failed to control acid secretion. Thirteen patients were found to have primary gastrinomas of the duodenum and an additional 13 patients had islet cell hyperplasia without evidence of frank neoplasm; prognosis in these two groups appears to be particularly favorable. Despite the current availability of effective nonoperative measures for control of gastric hypersecretion, surgical exploration is warranted in all patients to determine location and extent of tumor and to attempt to control the ulcer diathesis by resection of tumor. Long-term therapy with H2 receptor antagonists is advised for patients whose hypersecretory state has not been alleviated by tumor resection or whose gastrinoma cannot be removed. Total gastrectomy is still indicated in patients whose tumors are not amenable to resection and who are resistant to, or cannot follow, a rigid medical regimen. (Author abstract) (20 Refs)

ECTOPIC HORMONE PRODUCTION BY NON ENDOCRINE TUMORS

48. ROENTGENOLOGIC DIAGNOSIS OF PRIMARY CORTICOTROPIN-PRODUCING CARCINOID TUMORS OF THE MEDIASTINUM.

Brown LR, Aughenbaugh GL, Wick MR, Baker BA, Salassa RM
Mayo Clinic, Rochester, MN, 55905
Radiology; 142(1):143-148 1982

A study was undertaken of five patients with Cushing syndrome due to ACTH production by thymic carcinoid tumors (primary mediastinal APUDomas), including two recent patients examined by computed tomography (CT) of the chest. Plain roentgenography of the chest initially failed to detect tumor in four of the five patients, while CT of the chest yielded definitive diagnostic information in both patients in whom it was employed. For one of these patients, a mediastinal tumor could be seen retrospectively on plain roentgenograms of the chest, although it had been missed on the first examination. One of the tumors appeared to be partially calcified on CT scan, a finding not previously reported. Blastic osseous metastasis, which is common when malignant carcinoid tumors spread to bone, was seen in one patient. Our data suggest that in patients with suspected ectopic ACTH production, CT scanning of the mediastinum should be performed early in order to avoid delay in diagnosis of an ACTH-secreting carcinoid tumor of the mediastinum. (Author abstract) (20 Refs)

49. BIOCHEMICAL AND IMMUNOLOGICAL CHARACTERIZATION OF ECTOPIC TUMORAL RENIN.

Soubrier F, Devaux C, Galen FX, Skinner SL, Aurell M, Genest J, Menard J, Corvol P
INSERM U36, 17, rue du Fer-a-Moulin, 75005 Paris, France
J Clin Endocrinol Metab; 54(1):139-144 1981

Biochemical and immunological characteristics of renin secreted by two malignant renin-secreting tumors [pulmonary (PT) and paraovarian (POT)] were studied. They both contain inactive renin (IR), as renin activity of tumoral extracts was able to be increased after acid activation or trypsin treatment (10.1 to 20.8 Goldblatt units/g tissue for PT and 3.4 to 3.7 for POT). Renin activity after activation reached the value obtained by direct RIA of human renin (23 and 3.6, respectively), as both forms are recognized by renin antiserum. Both enzymatic activities could be completely inhibited by renin antiserum. Displacement curves for the two tumoral renins paralleled the ARC curve in the direct RIA. After chromatography on affigel-blue, active renin was not bound to the gel, and inactive renin eluted only with 1 M NaCl. On pepstatin-Sepharose and CH-pepstatin-Sepharose (an A-modified pepstatin), a separation of the two forms of pulmonary renin was obtained; inactive renin eluted with breakthrough proteins, whereas active renin was strongly bound to the gel. After this affinity chromatography, the mol wt of inactive and active renin, determined on Ultrogel, were very close (46,000 and 45,500). We conclude that (1) ectopic renin in these cases is similar to the renal enzyme; (2) renin can be secreted in an inactive form, supporting the hypothesis of an inactive initial state of renin; and (3) mol wt differences between the two forms are very slight. (Author abstract) (25 Refs)

50. NEUROENDOCRINE DIFFERENTIATION IN BASAL CELL CARCINOMAS.

Hardt LE, Memoli VA, Gould VE
(c/o Gould) Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL 60612
J Cutan Pathol; 8(5):335-341 1981

Ten consecutive cases of basal cell carcinomas were reviewed. Nine of these displayed the typical histology of basal cell carcinoma, the other case was composed of small spindle to ovoid cells with scant cytoplasm and a high mitotic rate, resembling an 'oat cell' carcinoma. These were studied using the immunoperoxidase technique for tissue localization of calcitonin, insulin, glucagon, somatostatin, ACTH, gastrin and nerve growth factor. Three cases were negative for all hormones tested. Three cases were focally positive for a single hormone; one each for calcitonin, somatostatin, and ACTH. Two cases were focally positive for ACTH and somatostatin and two cases were focally positive for calcitonin, somatostatin and ACTH. None of the other hormones displayed activity. The positive staining was eliminated after absorption by the specific antigen. This immunohistochemical study illustrated neuroendocrine differentiation in basal cell carcinomas as has previously been suggested by the Grimelius stain and electron microscopy. Thus, as demonstrated in other epithelial neoplasms, basal cell carcinoma may also display neuroendocrine differentiation. This illustrates the potential multidirectional differentiation in neoplastic epithelial cells. (Author abstract) (23 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

51. COMPARATIVE STUDY OF HUMAN FETAL, NORMAL ADULT, AND SOMATOTROPIC ADENOMA PITUITARY FUNCTION IN TISSUE CULTURE.

Marcovitz S, Goodyer CG, Guyda H, Gardiner RJ, Hardy J
Div. Endocrinology, Montreal General Hosp., 1650 Cedar Ave., Montreal H3G 1A4, Canada
J Clin Endocrinol Metab; 54(1):6-16 1982

Tissue from 14 somatotropic adenomas, 2 normal adult pituitaries, and 16 fetal pituitaries (10-20 weeks gestation) was maintained in culture for 2 weeks. The secretion of GH, PRL, LH, and TSH into culture medium was studied both in the basal state and in response to acute (2 h) exposure to TRH, apomorphine, somatostatin (SRIF), LRH, and theophylline. The findings were compared with results of in vivo dynamic pituitary function tests performed in the adult patients before transsphenoidal surgery. Several conclusions were reached: (1) TRH may be a physiological regulator of GH secretion; its paradoxical effect in acromegaly appears to be caused by an alteration at the level of the tumor cell. (2) The direct effect of apomorphine on normal pituitary tissue is a suppression of both GH and PRL secretion; the paradoxical GH suppression observed in vivo in some acromegalics is due to an alteration of the extrapituitary action(s) of apomorphine; on the other hand, nonresponsiveness of this dopaminergic agent seems to be caused by a change in the adenoma cell itself. (3) SRIF suppresses GH secretion from the normal pituitary and adenoma tissue in an identical manner. (4) The abnormalities observed in the adenomas generally do not appear to be a reversion toward the fetal state. (46 Refs)

52. A NEW IN VITRO ASSAY FOR HUMAN THYROID STIMULATOR USING CULTURED THYROID CELLS: EFFECT OF SODIUM CHLORIDE ON ADENOSINE 3',5'-MONOPHOSPHATE INCREASE.

Kasagi K; Konishi J; Iida Y; Ikekubo K; Mori T; Kuma K; Torizuka K
(c/o Konishi) Dept. Nuclear Medicine, Kyoto Univ. Sch. Medicine, Shogoin, Sakyo-ku, Kyoto 606, Japan
J Clin Endocrinol Metab; 54(1):108-114 1982

A new sensitive in vitro assay for human thyroid stimulator (HTS) was developed using human thyroid adenoma cells in monolayer culture. After being cultured for 2 days, the cells were incubated in 0.3 ml Hank's solution without 0.8% NaCl (medium 1) and with thyroid stimulator (bovine TSH or 3 mg patient serum immunoglobulin G) at 37 C for 2 hr. The cAMP generated in the cells and the medium during the incubation was measured by RIA. The assay was sensitive enough to elicit a 1.7-to 7.9-fold increase in cAMP at a TSH concentration of 10 uU/ml. HTS was detected in 33 (82.5%) of the 40 patients with untreated Graves' disease using this assay system. In Hank's solution (medium 2), however, HTS was detected in only 5 (23.8%) of the 21 patients with untreated Graves' disease. cAMP increment upon stimulation by either TSH or HTS in medium 1 was larger than that in medium 2, and the difference in the response to HTS using the two media was much greater than that in the response to TSH. Therefore, all HTS-immunoglobulin G studied showed higher activity using medium 1 than using medium 2 when expressed as bovine TSH equivalent. Analysis by the Lineweaver-Burk plot of dose-response curves of the effect of TSH and HTS stimulation on cAMP increment showed an increase in the Km upon the addition of NaCl to the medium. A similar inhibitory effect of NaCl (150 mM) was also observed in the assay system of human thyroid adenylate cyclase stimulator using crude plasma membrane fractions. In summary: (1) an assay for HTS measuring cAMP production in cultured thyroid adenoma cells was developed, and the assay using low NaCl medium was found to be the most sensitive; and (2) the inhibitory effect of NaCl on the response to HTS was much greater than that on the response to TSH. These data suggest different behaviors of these two stimulators at their receptor sites. (Author abstract) (26 Refs)

53. ABNORMAL REGULATION OF PARATHYROID HORMONE RELEASE BY CALCIUM IN SECONDARY HYPERPARATHYROIDISM DUE TO CHRONIC RENAL FAILURE.

Brown EM; Wilson RE; Eastman RC; Pallotta J; Marynick SP
Endocrine-Hypertension Unit, Brigham and Women's Hosp., 75 Francis St., Boston, MA 02115
J Clin Endocrinol Metab; 54(1):172-179 1982

Dispersed parathyroid cells were employed to study calcium-regulated parathyroid hormone (PTH) release in severe secondary hyperparathyroidism due to chronic renal insufficiency. Cell preparations were obtained from 16 parathyroid glands of six patients undergoing subtotal parathyroidectomy for parathyroid bone disease and/or hypercalcemia. The effects of increasing ambient calcium concentration on immunoreactive PTH release in vitro were assessed and compared with results observed in cells prepared from seven adenomas and six normal parathyroid glands. There was no difference in maximal PTH release for the three types of tissue (mean ± SEM, 8.48 ± 1.9, 8.1 ± 3, and 10.1 ± 0.78 ng/10(5) cells/hr respectively). In 14 of 16 hyperplastic glands, 6 of 7 adenomas, and all of the normal glands, PTH release was inhibited more than 50% by 2.1 mM calcium (suppressible glands). Of the normal glands, half of the maximal inhibition of PTH release (the set-point) occurred at less than 1.03 mM calcium in five of six cases. In 12 of 14 suppressible hyperplastic glands and all of the 6 suppressible adenomas, on the other hand, the set-point was 1.03 mM or higher (p less than 0.01 and p less than 0.002, respectively). Thus, in severe secondary parathyroid hyperplasia due to chronic renal insufficiency, there is frequently an increase in the set-point for calcium without a change in the maximal secretory rate per cell. Abnormal calcium-regulated PTH release at the cellular level, therefore, is not limited to parathyroid neoplasia (ie adenoma of primary hyperplasia), but may occur in secondary hyperplasia as well. (Author abstract) (34 Refs)

54. HETEROGENEOUS FORMS OF THYROID-STIMULATING HORMONE IN MOUSE THYROTROPIC TUMOR AND SERUM: DIFFERENCES IN RECEPTOR-BINDING AND ADENYLATE CYCLASE-STIMULATING ACTIVITY.

Pekonen F, Carayon P, Amr S, Weintraub BD
(c/o Weintraub), NIH, Building 10, Room 8N315, Bethesda, MD, 20205
Horm Metab Res; 13(11):617-620 1981

Thyroid-stimulating hormone (TSH) in tumor and serum of mice with thyrotropic tumors was studied by radioimmunoassay (RIA), radioreceptor assay (RRA) and thyroid adenylate cyclase assay (ACA). In unfractionated samples, serum TSH displayed significantly higher ACA/RIA (0.69 +-0.10) and ACA/RRA ratios (0.79 +-0.04) than TSH in tumor extracts (0.45 +-0.05 and 0.31 +-0.01, respectively). After gel chromatography, both tumor and serum TSH activity measured in RIA and RRA eluted in broad, heterogenous peaks with an apparent mol wt range of 26,000-44,000 daltons. The ACA activity of tumor TSH eluted in two sharp peaks (26,000 and 44,000) while that of serum TSH eluted in three peaks (26,000, 33,000 and 44,000). The ACA/RIA and ACA/RRA ratios varied greatly among the chromatography fractions, the lowest ratios being detected in the tumor TSH of 33,000 daltons (0.02 for each) and the highest ratios in both tumor and serum TSH of 26,000 (ACA/RIA = 1.60-1.90, ACA/RRA = 1.12-1.20). Since previous biosynthetic studies have suggested that such heterogeneous forms of mouse tumor TSH differ solely in carbohydrate content, our data suggest that the biologic activity of TSH may be modulated by its glycosylation. (Author abstract) ([illegible] Refs)

55. SOMATOSTATIN ELABORATION BY MONOLAYER CELL CULTURES DERIVED FROM TRANSPLANTABLE RAT MEDULLARY THYROID CARCINOMA: SYNERGISTIC STIMULATORY EFFECTS OF GLUCAGON AND CALCIUM.

Aron DC, [illegible], Birnbaum RS, [illegible], Roos BA
Endocrinology and Mineral Metabolism, Veterans Admin. Medical Center, Case Western Reserve Univ., 10701 East Boulevard, Cleveland, OH, 44106
Endocrinology; 109(6):1830-1834 1981

Somatostatin (SRIF)-producing transplantable rat medullary thyroid carcinomas (MTCs) were used to establish primary monolayer cell cultures for studying SRIF secretion and production. Immunoreactive SRIF (iSRIF) and calcitonin (iCT) levels in the MTC cell cultures were 152 and 4,900 ng/mg cell protein, respectively. The acute effects of calcium and glucagon on the elaboration of iSRIF and iCT were investigated in 3-hr experiments. Basal secretion rates (mean +- SE, five experiments) for iSRIF and for iCT were 10.7 +-2.5 and 297 +-33 ng/mg cell protein, respectively. Calcium stimulated the secretion of iSRIF and iCT in dose-dependent fashion. Maximal secretory effect of calcium was observed at 4.5 mM: iCT secretion increased 148% over basal, and iSRIF secretion increased 228% over basal. At 1 mM calcium, maximally effective doses of glucagon (1 uM) significantly increased iCT secretion (44% over basal) but not iSRIF secretion. At 5 mM calcium, as little as 10 nM glucagon had a significant stimulatory effect on secretion of both peptides. The largest stimulation was observed at 5 mM calcium and 1 uM glucagon; for iSRIF a 527% increase over basal and for iCT and 308% increase over basal were observed under this condition. At high calcium the stimulatory effect of glucagon on iSRIF secretion and on iCT secretion was significantly greater than at low calcium. In these 3-hr experiments neither 5 mM calcium nor 1 uM glucagon increased culture content (cells plus medium) of iCT or iSRIF. However, 3-hr treatment of the cell cultures with both agonists increased total culture content of iSRIF by 53% and iCT by 21%. The establishment of SRIF-producing cell cultures from transplantable rat MTCs and the identification of a synergistic secretagogue interaction for glucagon and calcium open the way for systematic in vitro investigation of SRIF secretion and biosynthesis. (Author abstract) (27 Refs)

56. CALCITONIN INDUCTION OF A PERSISTENT ACTIVATED STATE OF ADENYLATE CYCLASE IN HUMAN BREAST CANCER CELLS (T 47D).

Lamp SJ, Findlay DM, Moseley JM, Martin TJ
(c/o Martin) Dept. Medicine, Univ. Melbourne, Repatriation General Hosp., Heidelberg, Victoria 3081, Australia
J Biol Chem; 256(23):12269-12274 1981

In a calcitonin-responsive human breast cancer cell line (T 47D), specific receptors exist for calcitonin in intact cells, which show saturable binding which is only slowly and incompletely reversible. Full stimulation of cyclic AMP production in the cells was achieved with less than 50% receptor occupancy. Pretreatment of cells in culture with calcitonin, followed by washing, led to loss of adenylate cyclase response to calcitonin in homogenates. This took place rapidly, reaching a maximum after 15 min of preincubation with 1 nM salmon calcitonin, and was associated with a substantial increase in basal adenylate cyclase activity, which was dose-dependent and agonist-specific, in that it did not occur upon treatment of the cells with prostaglandin E2. Recovery was accompanied by recovery of specific binding of [125I]calcitonin to intact cells. This took place more slowly, requiring at least [illegible] for completion. Recovery of adenylate cyclase responsiveness and return of basal activity to normal was a relatively slow process, always requiring more than 24 h for completion. Neither the desensitization nor the persistent basal activity could be transferred to the cytosol compartment of calcitonin-preincubated cells. When calcitonin-preincubated cells were washed, and at intervals thereafter, the production of cyclic AMP was measured in the presence of a phosphodiesterase inhibitor, a 120-fold rise in basal cyclic AMP production was observed, and the response to added calcitonin was lost. Return of basal activity and of calcitonin responsiveness followed a time course similar to that seen in recovery of adenylate cyclase response. The results indicate the ability of calcitonin to induce rapidly a persistent state of adenylate cyclase activation which remains stable for several hours. This may be due to persistent tight binding of calcitonin but may also be related to changes induced by calcitonin in availability or function of nucleotide regulatory units. (Author abstract) (34 Refs)

57. EFFECT OF AN LHRH ANALOG ON GROWTH AND HORMONE RECEPTOR LEVELS IN DMBA-INDUCED MAMMARY TUMORS IN THE RAT.

Turcot-Lemay L, Cusan L, Seguin C, Kelly P, Labrie F
Dept. Molecular Endocrinology, Le Centre Hospitalier de l'Universite Laval, Quebec G1V 4G2, Canada
J Recept Res; 2(2):135-151 1981

Hormone-dependency of dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in rats was studied. Daily injections of luteinizing hormone-releasing hormone (LHRH) agonist, [D-Ala(6), des-Gly-NH2(10)]LHRH ethylamide (LHRH-A), 1 ug/day, for 38 days resulted in a 35% decrease in the number of tumors present at the start of the experiment compared to decreases of 45% after ovariectomy and of 8% in the control group. Although LHRH-A administration resulted first in a stabilization in the number of tumors, a marked inhibitory effect of the LHRH agonist on total tumor mass/rat was observed. There was marked reduction in ovarian luteinizing hormone (LH) and follicle-stimulating hormone (FSH) receptors while prolactin receptors were unchanged. Estrogen and progesterone receptor levels decreased after ovariectomy but treatment with LHRH-A had no significant effect on these receptors. Plasma LH and FSH levels increased after ovariectomy. Treatment with LHRH-A was followed by similar but less marked increases in plasma LH and FSH, with significant decrease in plasma prolactin and progesterone levels. The mechanisms by which LHRH-A induces the antitumor effect probably is related to desensitization of the ovary to LH and FSH with a concomitant decrease in circulating levels of estrogen and prolactin. (21 Refs)

58. NEURON SPECIFIC ENOLASE IN HUMAN SMALL CELL CARCINOMA CULTURES.

Marangos PJ, Gazdar AF, Carney DN
Clinical Psychobiology Branch, NIMH, Bldg. 10, Room 4S239, 9000
Rockville Pike, Bethesda, MD, 20205
Cancer Lett; 15(1):67-71 1982

Continuous cell lines of human lung cancer were analyzed for neuron specific enolase (NSE). The levels of NSE were determined in 21 cell culture samples derived from patients with small cell carcinoma of the lung (SCCL) and in [illegible] derived from patients with non-SCCL. The non-SCCL tumors were [illegible] adenocarcinomas, [illegible] large cell carcinomas, a squamous cell carcinoma, and a [illegible] tumor. NSE levels in the cells derived from small tumors are in every case except one higher than those derived from non-small cell tumors with the mean value of [illegible] nanog/mg protein. SCCL cells studied possess only amine precursor uptake and decarboxylation (APUD) cell characteristics as high levels of dopa decarboxylase and neurosecretory granules that they are distinct from other forms of lung cancer. NSE is strictly localized to neurons and neuroendocrine cells of the APUD series. NSE is present at much higher levels in the cultures derived from SCCL cells. The amounts of NSE present in the cultured SCCL cell lines ranged from 106-5071 nanog/mg protein. The highest value observed indicates that NSE represent 0.5% of the total soluble protein in the studied culture. Preliminary results concerning NSE levels in sera of patients with SCCL indicate that the levels of this protein may be useful in staging and following the course of the disease. (15 Refs)

59. NEUROPHYSIN BIOSYNTHESIS IN VITRO IN OAT CELL CARCINOMA OF THE LUNG WITH ECTOPIC VASOPRESSIN PRODUCTION.

Yamaji T, Ishibashi M, Katayama S, Itabashi A, Ohsawa N, Kondo Y, Mizumoto Y, Kosaka K
Third Dept. Internal Medicine, Univ. Tokyo, Hongo, Tokyo 113, Japan
J Clin Invest; 68(6):1441-1449 1981

The incorporation of labeled compounds into neurophysins of a transplantable human oat cell carcinoma of the lung with ectopic vasopressin production was studied in vitro. Neurophysins in cell extracts and in incubation media were isolated by immunoprecipitation and analyzed by sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis. When cells were incubated with L-[35S]cysteine for 12 hr, SDS-polyacrylamide gel electrophoresis of the immunoprecipitates from cell extract and medium resolved two forms of neurophysins with apparent mol mass of 10,000 (10K) and 20,000 (20K). Both forms of [35S]neurophysins were completely displaced from the immunoprecipitates by excess human neurophysin. Incubation of cells with L-[35S]cysteine and D-[3H]glucosamine hydrochloride revealed that glucosamine was incorporated into the 20K neurophysin region, but not into 10K species. To observe the kinetics of labeling of the two forms of neurophysins, cells were incubated with L[35S]cysteine for varying periods of time. After short labeling periods, most of the radioactivity resided in 20K species, which plateaued after 1 hr, whereas 10K neurophysin progressively increased in its height. When cells were chased with unlabeled cysteine after the exposure to a short pulse of labeling, 20K neurophysin peak gradually decreased with an apparent initial half-life of 1 hr. In contrast, the label in 10K neurophysin steadily increased, which exceeded the former by 3 hr of chase. Analysis of 20K neurophysin in cell extract by isoelectric focusing on polyacrylamide gel demonstrated that it was principally composed of a protein with an apparent isoelectric point (pI) of [illegible]. These results suggest that neurophysin is synthesized in ectopic vasopressin-producing tumors by posttranslational processing from a glycosylated proneurophysin with an apparent molecular mass of 20,000 daltons and a pI of [illegible]. (Author abstract) (22 Refs)

60. MECHANISMS OF BONE REMODELING INDUCED BY TUMORS: TUMOR HUMORS.

Tashjian AH
Lab. Toxicology, Harvard Sch. Public Health, Boston, MA, 02115
Schweiz Med Wochenschr; 111(49):1868-1873 1981

Mechanism of bone remodeling (BR) by tumor-induced alterations is reviewed. BR may be altered by the presence of metastatic tumor in bone, by the synthesis and release into circulation of humoral factors by tumor cells, or by syndromes with hypercalcemia. Cell culture and animal studies indicate that tumor cells secrete humoral factors, such as parathyroid hormone, which produce hypercalcemia. Animal studies with HSDM1 and VX2 tumors show that these tumors produce excessive amounts of prostaglandin E2 (PGE2), which stimulates bone resorption. PGE2 activity is inhibited by low concentrations of indomethacin (IM) or hydrocortisone (HC). IM and HC prevent or reverse hypercalcemia in tumor-bearing animals. High levels of PGE2 in venous drainage of tumors indicates the tumors as the source of PGE2. The effects PGE2 are systemic and are not confined to the area of the tumor or metastases. Studies in mice show that epidermal growth factor (EGF) and platelet-derived growth factor (PDGF) enhance metabolism of arachidonic acid, which can be metabolized to PGE2 by bone cells. EGF and PDGF may be produced by tumor cells. Understanding the effects of humoral factors on BR should facilitate proper therapy for tumor-related conditions. (38 Refs)

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Consulting reviewer:
NAGUIB A. SAMAAN, M.D., Ph.D.

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. THE CLINICAL IMPLICATIONS OF DNA CHARACTERISTICS IN HUMAN PITUITARY TUMOUR DISEASE.

Anniko M, Holm LE, Tribukait B, Werner S, Wersall J
Dept. Otolaryngology, Karolinska Hosp., S-104 01 Stockholm, Sweden
Acta Otolaryngol [Suppl] (Stockh): (379):21-28 1981

DNA analysis was performed in 29 cases of various endocrinological types of human pituitary tumors. The degrees of

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ploidy and proliferation, expressed as the proportion of cells in S phase, were determined. In 12 cases (41%) aneuploidy occurred. The proportion of aneuploid cells in these tumors was very high, in general around 95% measured. The aneuploid group of pituitary tumors showed a large variation of the percentage of cells in S-phase (range: 3.3-13.7%; mean: 8.3 +-5.3) in contrast to diploid tumors which showed a considerably smaller variation (range: 3.4-8.8%; mean 5.5 +-2.1). Patients with aneuploid tumors had a mean age at operation of 42.8 +-11.1 yr in contrast to 51.5 +-13.8 yr for patients with diploid tumors. Aneuploidy occurred more frequently in tumors causing acromegaly with a concomitant secretion of GH and PRL than in other endocrinological types of tumors. Patients with aneuploid tumors had a mean case history of 2.9 +-1.9 yr, as compared to 10.5 +-4.9 yr for patients with diploid tumors. In many cases, tumors with an aneuploid DNA pattern caused a high clinical activity of acromegaly. (Author abstract) (28 Refs)

2. CORTICOLIPOTROPIN IMMUNOREACTIVITY IN SILENT CHROMOPHOBE ADENOMAS: A LIGHT AND ELECTRON MICROSCOPIC STUDY.

Hassoun J, Charpin C, Jaquet P, Lissitzky JC, Grisoli F, Toga M
Laboratoire d'Anatomie Pathologique et de Neuropathologie, 27, Bd Jean Moulin, 13885 Marseille Cedex V, France
Arch Pathol Lab Med; 106(1):25-30 1982

Twenty silent human pituitary adenomas were morphologically studied. Immunoperoxidase methods showed numerous adrenocorticotropic hormone-immunoreactive tumor cells in 14 cases by light microscopy and in one additional case by electron microscopy. Three of these cases were positive for beta-endorphin and one for beta-lipotropin by electron microscopy. These immunoreactions were found in undifferentiated tumors as well as in oncocytic adenomas, and could not be related to the presence of basophils by light microscopy. The peptides so detected in silent adenomas may have no biological activity and may correspond to common precursor molecule subunits. (Author abstract) (35 Refs)

3. HUMAN PITUITARY GONADOTROPIC ADENOMA; HISTOLOGICAL, IMMUNOCYTOCHEMICAL, AND ULTRASTRUCTURAL AND HORMONAL STUDIES IN EIGHT CASES.

Trouillas J, Girod C, Sassolas G, Claustrat B, Lheritier M, Dubois MP, Goutelle A
(c/o Girod) Laboratoire d'Histologie, Faculte de Medicine Alexis Carrel, Rue Guillaume Paradin, F-69372 Lyon Cedex 2, France
J Pathol; 135(4):315-336 1981

Histological, immunocytochemical, ultrastructural, and hormonal characteristics of human pituitary gonadotropic adenoma (PGA) were studied. In a series of 230 surgically removed pituitary adenomas, 8 had increased intratumor levels of gonadotropins and showed positive immunostaining for gonadotropic cells. Examination by light microscope showed all eight tumors to be composed of agranular cells that were generally PAS-negative. Immunofluorescent staining demonstrated immunoreactive follicle stimulating hormone (FSH) beta-subunits alone in two tumors, and FSH and luteinizing hormone (LH) in six tumors, of which two had immunoreactive FSH beta-subunits. Electron micrographs showed moderately or well developed endoplasmic reticulum that was frequently dilated. Also present were secretory granules of varying electron density and numerous microtubules. Hormonal analysis showed elevation of basal plasma levels FSH and LH in two cases and FSH alone in two cases. FSH and LH plasma levels were approx normal in three cases. Analysis of intratumor hormone levels showed elevated FSH and LH in five cases and FSH alone in two cases. Elevated FSH beta-endorphin was found in two cases. Other hormone levels were insignificant in all cases. Immunoreactivity of tumors correlated well with hormone levels in the tumors. Results suggest three types of PGA producing FSH alone, FSH and LH, or FSH, LH, or immunoreactive beta-endorphin. (56 Refs)

4. ACTH SECRETING PITUITARY ADENOMA IN AN INFANT OF 18 MONTHS. IMMUNOHISTOCHEMICAL, ELECTRON- MICROSCOPIC, AND IN-VITRO STUDIES.

Saeger W, Ruttmann E, Ludecke D
(c/o Saeger) Abteilung fur Pathologie, Marienkrankenhaus, Alfredstr. 9, 2000 Hamburg 76, W. Germany
Pathol Res Pract; 173(1/2):121-129 1981

An 18-mo old infant with Cushing's disease due to an ACTH producing pituitary tumor is presented. The case showed typical clinical and morphological signs of hypercortisolism. The infant died of pulmonary thrombembolism after transsphenoidal partial adenomectomy. The adrenals were diffusely hyperplastic. The pituitary adenoma was classified as an undifferentiated mucoid cell adenoma with sparse granulation by light microscopy. Immunoenzymatic studies demonstrated ACTH not only in granulated adenoma cells. Ultrastructurally the cells were only differentiated as typical ACTH cells or so-called follicular cells in small areas. Most of them were undifferentiated, showing pleomorphism of the relatively sparse organelles. In-vitro experiments using suspensions of adenoma cells showed a distinct enhancement of ACTH secretion after arginine-vasopressin and a further decrease ultrastructurally in the number of secretory granules. No effect on ACTH levels and no alterations of the ultrastructure were observed after cortisol. The case is representative of typical hypothalamic-hypophyseal Cushing's disease with an undifferentiated pituitary adenoma secreting ACTH in part autonomously. This constellation of Cushing's syndrome is extremely rare at the age of 1 yr. Our case is the second one reported in the literature. (Author abstract) (17 Refs)

5. TREATMENT OF HYPERPROLACTINEMIC STATES WITH DIFFERENT DRUGS: A STUDY WITH BROMOCRIPTINE, METERGOLINE, AND LISURIDE.

Crosignani PG, Ferrari C, Liuzzi A, Benco R, Mattei A, Rampini P, Dellabonzana D, Scarduelli C, Spelta B
Fourth Dept. Obstetrics and Gynecology, Univ. Milan, Via Melloni 52, Milan, Italy
Fertil Steril; 37(1):61-67 1982

One hundred ninety-one hyperprolactinemic patients (178 women and 13 men; 54 with pituitary macroadenoma, 53 with microadenoma, and 84 with idiopathic disease) were treated for 2 to 48 mo with one or two of the following prolactin (PRL)-lowering drugs: bromocriptine, metergoline, and lisuride. All of the three drugs used were highly effective in lowering PRL levels and restoring gonadal function both in females and in males in the majority of patients with either idiopathic or tumorous disease. In poorly responsive patients, increasing the drug doses resulted in further PRL lowering for all the three drugs. Mild side effects were frequently encountered with initiation of drug treatment but spontaneously subsided in most cases; severe side effects, necessitating stopping of the treatment, occurred in only 12 instances, but changing of the drug allowed PRL-lowering treatment to be continued in 11 of them. (Author abstract) (21 Refs)

6. CLINICAL TRIAL OF THE SIZE-REDUCING EFFECT OF BROMOCRIPTINE ON PITUITARY TUMORS.

Wollesen F, Andersen T, Karle A
Endokrinologisk afdeling, Kobenhavns kommunes hospital, DK-2650 Hvidovre, Denmark
Ugeskr Laeger; 143(52):3534-3538 1981

The effect of bromocriptine (BC) treatment on the size reduction of aggressively growing extrasellar solid pituitary tumors was studied in 20 consecutive patients (8 men and 12 women, 35-76 yr old). Twelve patients were pretreated, mostly by the combination of surgery and radiotherapy; the therapy-free interval of these 12 patients was 5-118 mo. Ten patients received hormone substitution therapy. BC was administered in daily doses of 15 mg (1 patient), 30 mg (12), 60 mg (6) and 160 mg (1) for 2-48 mo. The tumor size was determined by computed tomography before and during the BC treatment. The median absolute reduction of the tumor size was 36.5 square mm (mm2) from 94.5 mm2 to 59.5 mm2. The median relative reduction for all 20 patients was by 32%. Three tumors disappeared completely, 13 were reduced in size by 18-65%, 2 showed growth arrest and two continued to grow during the treatment. Reduction of tumor size or growth arrest occurred in 4/5 patients with normal prolactin secretion. The relative tumor size reduction was significantly and positively correlated with the pretreatment tumor size, but not to the serum levels of hormones, nor to the BC dose, length of treatment, and sex of the patients. The only major side-effect was a reduced need for early morning sleep in 8/20 patients. The immediate success rate of BC treatment in terms of tumor size reduction was of the same order of magnitude as that of the two conventional therapeutic modalities for large pituitary tumors. (15 Refs) (In DAN)

7. TUMORAL DEVELOPMENT OF PROLACTIN-SECRETING PITUITARY ADENOMAS DURING PREGNANCY. THERAPEUTIC APPROACHES.

Rohmer V, Strauch G, Luton JP, Bricaire H
(c/o Luton) Centre de Recherches Endocrinologique, Hopital Cochin, 27, rue du Faubourg Saint-Jacques, F 75674 Paris Cedex 14, France
Nouv Presse Med; 10(46):3783-3786 1981

During pregnancy the volume of prolactin-secreting pituitary adenomas tends to increase dangerously for surrounding structures, especially the optic chiasma. When rapid growth occurs, at least three therapeutic approaches are possible: resection of the adenoma, temporization under monitoring and administration of bromocriptine. The latter treatment, which seems to be of particular value, was applied to a female patient and was followed by prompt regression of optic chiasma compression. However, as bromocriptine was given concurrently with chlormadinone acetate, this excellent result cannot be ascribed to bromocriptine alone. (Author abstract) (21 Refs) (In FRE)

8. HYPERPROLACTINEMIA - THE UNDERLYING PHYSIOLOGY.

Maxson WS, Hammond CB
Vanderbilt Univ. Medical Center, Nashville, TN
Contemp Obstet Gynecol; 19(1):49-52,55-56,59,63 1982

The causes of hyperprolactinemia in neoplastic and non-neoplastic diseases are discussed. Prolactin levels fluctuate normally throughout a woman's life; prolactin is released episodically in pulses with a diurnal variation. The only certain functions of prolactin in humans are inducing development of the lobuloalveolar system of the breasts and initiating lactogenesis and milk secretion. High levels of estrogen and possibly prolactin inhibit lactation at the level of the breast. A variety of drugs may stimulate prolactin synthesis and secretion. Neoplastic causes of hyperprolactinemia include (1) inhibition of prolactin inhibiting factor (PIF) by hypothalamic tumors or pineal tumors (either primary or metastatic), (2) interruption of PIF transport due to pituitary stalk compression subsequent to hypothalamic or pituitary tumors, and (3) prolactin-secreting tumors, ie acromegaly, Cushing's disease, Nelson's disease, or microadenoma or macroadenoma of the pituitary, and ectopic tumor production from breast or bronchogenic carcinoma or hypernephroma. (31 Refs)

9. CUSHING'S DISEASE: TRANSIENT SECONDARY ADRENAL INSUFFICIENCY AFTER SELECTIVE REMOVAL OF PITUITARY MICROADENOMAS; EVIDENCE FOR A PITUITARY ORIGIN.

Fitzgerald PA, Aron DC, Findling JW, Brooks RM, Wilson CB, Forsham PH, Tyrrell JB
Metabolic Res. Unit, Univ. California,, 1143 HSW, San Francisco, CA, 94143
J Clin Endocrinol Metab; 54(2):413-422 1982

Of 12 patients with Cushing's disease who had successful selective microadenoma resection documented by clinical remission and reversal of hypercortisolism, 11 developed postoperative hypoadrenalism with deficient adrenal responsiveness to exogenous ACTH. The ACTH and glucocorticoid deficiency was not caused by the surgical procedure or hydrocortisone replacement, since it resolved despite replacement therapy; further, adrenal insufficiency did not occur in 10 acromegalic patients who received the same operation and identical glucocorticoid therapy. Other pituitary functions were not impaired postoperatively. We conclude that (1) the hypercortisolism caused by an ACTH-secreting pituitary microadenoma suppresses the normal pituitary secretion of ACTH and often that of GH and LH; (2) this suppression persists postoperatively, but gradually resolves in most patients; (3) a normal cortisol response to ACTH is a good indication that the pituitary-adrenal axis has recovered; (4) there is no evidence of a persisting hypothalamic defect after removal of ACTH-secreting microadenomas; and (5) pituitary microadenomas appear to be the primary cause of Cushing's disease in these patients. (65 Refs)

10. ADRENOCORTICOTROPIN-SECRETING PITUITARY ADENOMAS ORIGINATE FROM THE ANTERIOR OR THE INTERMEDIATE LOBE IN CUSHING'S DISEASE: DIFFERENCES IN THE REGULATION OF HORMONE SECRETION.

Lamberts SW, De Lange SA, Stefanko SZ
Dept. Medicine III, Univ. Hosp. Dijkzigt, 40 Dr. Molewaterplein, 3015 GD Rotterdam, The Netherlands
J Clin Endocrinol Metab; 54(2):286-291 1982

The reactions to bromocriptine in patients with Cushing's disease was correlated with pathological examination of the pituitary adenomas and the outcome of transsphenoidal operation. Fifteen consecutive patients with Cushing's disease were operated upon, and pituitary tumor tissue was removed. In nine tumors, no neural tissue was present in the adenomas (Group I), but in the tissue removed from the other six patients, argyrophilic nerve fibers coursed freely through the adenoma tissue (Group II). In two the these six patients, multiple adenomatous and/or hyperplastic cell nests containing nervous tissue were present, while a localization of tumor tissue in the intermediate lobe of the pituitary gland was evident in three of them. Differences between the two groups of patients are presented. We hypothesize that Cushing's disease in man originates from two different locations. Most of the ACTH-secreting pituitary adenomas are located in the anterior part of the pituitary gland and can easily be removed during transsphenoidal operation. Part of the ACTH secreting pituitary adenomas are, however, intermediate lobe tumors containing nervous tissue. Multiple microadenomas and/or hyperplastic cell nests can be present in some of these patients, and transsphenoidal operation is less successful. This type of adenoma might be recognized by the demonstration of a suppression of plasma ACTH in response to bromocriptine and a lowered sensitivity to dexamethasone. (28 Refs)

11. LOWERING PROLACTIN LEVEL IN A HYPERPROLACTINEMIC MAN: RESPONSES OF LUTEINIZING HORMONE, FOLLICLE-STIMULATING HORMONE, AND TESTOSTERONE.

Davis JL
Dept. Internal Medicine, Naval Regional Medical Center, San Diego, CA, 92134
Arch Intern Med; 142(1):146-148 1982

A 25-year-old man with hypogonadotropic hypogonadism and elevated prolactin levels, presumably from a microadenoma of the pituitary gland, was treated with bromocriptine mesylate. After 3 weeks, the prolactin level had fallen and the gonadotropin levels had shown a substantial rise, reaching supraphysiologic levels by 8 weeks, eventually returning to normal by 15 weeks. The serum testosterone level did not rise until after 3 weeks and reached a maximum by 15 weeks. When the bromocriptine therapy was stopped for 1 week, all indexes returned to near pretreatment levels. Within 2 weeks of re-treatment with bromocriptine, the prolactin level had fallen and both testosterone and gonadotropin levels rose. These findings suggest that prolactin may block the secretion of luteinizing-releasing hormone, or may prevent the pituitary gland from responding to it. (Author abstract) (11 Refs)

12. POSTIRRADIATION SARCOMATOUS TRANSFORMATION OF A PITUITARY ADENOMA: A COMBINED PITUITARY TUMOR.

Pieterse S, Dinning TA, Blumbergs PC
(c/o Blumbergs), Inst. Medical and Veterinary Science, Box 14, Rundle St. Post Office, Adelaide 5000, South Australia
J Neurosurg; 56(2):283-286 1982

A case is reported in which a fibrosarcoma developed 20 yr after irradiation of a pituitary chromophobe adenoma. This rare lesion, like most of the other documented postirradiation pituitary sarcomas, was a combination of fibrosarcoma and pituitary adenoma. These lesions tend to behave in a characteristic fashion, with onset after a long latent interval following irradiation, growth to a large size, and failure to metastasize. (Author abstract) (13 Refs)

13. GRANULAR PITUICYTOMAS OF THE PITUITARY STALK.

Vaquero J, Leunda G, Cabezudo JM, Salazar AR, De Miguel J
Servicio de Neurocirugia, Clinica Puerta de Hierro, San Martin de Porres, 4, Madrid-35, Spain
Acta Neurochir (Wien); 59(3/4):209-215 1981

A case of suprasellar granular-cell tumor is presented. Only 27 other similar tumors in this location have been reported to date. These cases have been studied, and some clinical and radiological characteristics that are useful preoperatively are discussed. Regarding the pathological aspects, we have reviewed the various theories about the origin of these tumors and accept as the most plausible an origin from the granular pituicytes that can normally be found in the neurohypophysis and in the pituitary stalk. (Author abstract) (31 Refs)

14. BLOOD LEVELS OF BETA-ENDORPHIN AND BETA-LIPOTROPIN IN CUSHING'S DISEASE.

Slavnov VN, Valueva GV, Luchitskii EV, Iakovev AA
Lab. Radiology, Res. Inst. Endocrinology and Metabolism, Kiev, USSR
Ter Arkh; 53(12):107-110 1981

Blood levels of the neuropeptides beta-endorphin and beta-lipotropin were studied in 28 patients (17-52 yr old) with Cushing's disease (CD) and were compared with blood levels of corticotropin. The active stage of the CD was characterized by a significant increase in concentration of the neuropeptides. Normal blood levels of corticotropin were detected in 55% of the patients with active CD. Remission of the CD was characterized by normalization of the levels of the beta-endorphin and the beta-lipotropin. (12 Refs) (In RUS)

THYROID TUMORS

15. RADIOIODINE TOTAL BODY SCAN VERSUS SERUM THYROGLOBULIN LEVELS IN FOLLOW-UP OF PATIENTS WITH THYROID CANCER.

Colacchio TA, LoGerfo P, Colacchio DA, Feind C
Dept. Surgery, Coll. Physicians and Surgeons of Columbia Univ., New York, NY
Surgery; 91(1):42-45 1982

Two groups of patients were studied to compare the efficacy of serum thyroglobulin (Tg) levels to 131I total body scans in the follow-up of patients with thyroid cancer. All of the group of 30 patients without recurrence had undetectable Tg levels both on and off thyroid hormone replacement, and all had negative total body scan results although 8 patients, showed uptake in remnant thyroid tissue. In the second group of 37 patients with documented recurrent or metastasis disease, 34 (92%) had positive serum Tg levels, although the levels in 5 of these patients were undetectable while on thyroid replacement, and 31 (84%) had positive total body scan results. The false negative results of the two tests were not overlapping, and of those with positive Tg levels, 29 showed a significant increase once thyroid hormone therapy had been withdrawn. We conclude that although the percentages of positive Tg levels and body scan results in patients with recurrent disease are similar, both tests are required to minimize the number of patients with undiagnosed metastases. Second, thyroid-stimulating hormone suppression has a definite although unpredictable effect on serum Tg levels in patients with thyroid cancer, and thyroid hormone should be withdrawn prior to measurement of serum Tg to minimize the number of false negative results. (Author abstract) (13 Refs)

16. DIAGNOSIS OF THYROID CANCER IN TOXIC GOITER AND CHRONIC THYROIDITIS.

Myshkin KI, Bluvshtein GA, Lagun MA
Dept. Surgery, Medical Inst., Saratov, USSR
Sov Med; (11):92-94 1981

Cancer of the thyroid was diagnosed in 10/924 patients with toxic goiter and in 9/109 patients with chronic thyroiditis. Correct preoperative diagnosis of cancer of the thyroid was made after the transcutaneous puncture biopsy and histological examination. (9 Refs) (In RUS)

17. INTRAOPERATIVE CYTOLOGICAL DIAGNOSIS IN SURGERY ON THE THYROID GLAND.

Fabian E, Lukacs G, Csaky G, Balazs Gy
I. Sebeszeti Klinika, Debreceni Orvostudomanyi Egyetem, Debrecen, Hungary
Orv Hetil; 122(48):2943-2945 1981

Intraoperative cytological examinations were performed in 216 patients subjected to surgery for various diseases of the thyroid gland. The ultimate diagnosis was that of malignant tumor in 58 patients, benign adenoma in 28, thyroiditis in 22, regressive atypia in 4, hyperfunction in 19 and other nonmalignant diseases (ONMD) in 85. The results of the intraoperative cytological examinations were correct in 207/216 patients, incorrect in 9 (false positive in 7/9 and false negative in 2/9). The cytological findings were incorrect in 2/58 patients with malignant tumors, 3/28 with benign adenoma, 2/22 with thyroiditis, 1/4 with regressive atypia and 1/85 with ONMD. One malignant tumor was diagnosed correctly cytologically, but the histological finding was positive only on reoperation. The histological type of the malignant tumors, established in 57 cases, was papillary or mixed carcinoma in 26 cases, follicular carcinoma in 11, undifferentiated carcinoma in 10, medullary carcinoma in 2 and other malignant tumor in 8. Among the seven patients with false positive cytological diagnoses, follicular adenoma was diagnosed histologically in three, chronic thyroiditis in two, and regressive thyroiditis in one. Papillary or mixed carcinoma was diagnosed in one patient with histologically established metastatic follicular carcinoma. One of the 11 follicular carcinomas was diagnosed cytologically incorrectly as a benign tumor, while three follicular adenomas were incorrectly diagnosed cytologically as malignant tumors. (22 Refs) (In HUN)

18. THYROID CANCER.

Demidov VP, Voronetskii IB
Clinic Head and Neck Tumors, P. A. Hertsen Res. Oncological Inst., Moscow, USSR
Khirurgiia (Mosk); (11):57-61 1981

Of 1,500 patients with various thyroid diseases, 500 constituted a high risk group. Among the patients at risk, 28.8% had early thyroid cancer. Early cancer was detected in 30.8% of the patients with adenomas, 22.8% of the patients with chronic nonspecific thyroiditis, and 25% of the patients with nodular goiter. Early thyroid cancers had histology of follicular carcinoma (41.5%), follicular-solid carcinoma (23.6%), papillary carcinoma (27.4%), Hurtle cell carcinoma (4.7%), and C-cell carcinoma (2.8%). Diagnostic examination of the patients at risk for cancer included x-rays of the trachea, esophagus, lungs, and mediastinum, thyroid scintigraphy with radioactive iodine, thyroidolymphography, cytological examination of puncture specimens, and intraoperative express histological examination. At cytological examination, correct preoperative diagnosis was made in 62.5% of the patients. It was recommended that the patients with nodular goiter should be subjected to extrafascial hemithyroidectomy. (12 Refs) (In RUS)

19. OUR PROCEDURE FOR THYROID CANCER.

Essayag LR, Souto JV, Abella AF, Lupi JL, Buquet JA
Secc. Patol. de Cabeza y Cuello, Hospital Interzonal de Agudos, Aristobulo del Valle 1568 (1824), Lanus (Pcia. de Buenos Aires), Argentina
Prensa Med Argent; 68(13):527-529 1981

Of 432 patients with pathology of the thyroid gland, 324 had cold nodules, and of these, 82 (10 male, 72 female; 11-91 yr old, most 45-55 yr old) had thyroid cancer (TC). The time of evolution of the TC was 3 mo to 20 yr, and the main symptom was the presence of tumor. Treatment was based on results of biopsy performed at the time of surgery (needle biopsy was not used, due to difficulty in interpretation and danger of local dissemination), histologic examination, and presence or absence of lymph node involvement. Histologically, the tumors were papillary adenocarcinomas (48), follicular adenocarcinomas (19), undifferentiated (13), medullary (1), and Hurthle cell (1). Eight patients were inoperable; all others underwent total thyroidectomy. Cervical ganglionic metastases (ME) were removed in 21 patients. In patients who had undifferentiated TC with ME, cobalt therapy was administered; others received 131-iodine therapy. A table of times of evolution of the tumors in patients was presented. (12 Refs) (In SPA)

20. SURGICAL MANAGEMENT OF AUTONOMOUS ADENOMA OF THE THYROID GLAND.

Csaky G, Balasz Gy, Lukacs G, Fabian E, Kaposi T
I. Sebeszeti Klinika, Debreceni Orvostudomanyi Egyetem, Debrecen, Hungary
Orv Hetil; 123(1):15-18 1982

One hundred and twenty-three patients (108 women and 15 men) with autonomous thyroid adenoma were subjected to surgery. More than 2/3 of the patients were under the age of 50 yr. The symptoms included nervousness and sleep disorders in 119 patients, palpitation, tachycardia or arrythmia in 118, tremor and/or perspiration in 118, heat intolerance in 46 and loss of wt in 39. Only the patients with hyperthyroidism were prepared for the surgery. Enucleation was performed in 78.9% of the patients. The histomorphological findings showed nodular goiter with degenerative changes in 51 patients, hyperthyroidism in 46, adenoma in 35, chronic thyroiditis in 20, cyst in 5 and carcinoma in 2. Lobectomy with subtotal resection of the contralateral lobe was performed in the two carcinoma patients after primary enucleation. Immediately after surgery, tachycardia was seen in 35 patients and fever in 11. No cardiac complications were observed during the surgery and postoperative period. At 1 and 3 mo after surgery, 96% of the patients were subjectively symptom-free. The good results and lack of complications justify the surgical management of autonomous thyroid adenoma. (33 Refs) (In HUN)

21. COMPARISON OF 30-AND 50-MCI DOSES OF IODINE-131 FOR THYROID ABLATION.

Degroot LJ, Reilly M
Univ. Chicago, Box 138, 950 East 59th St., Chicago, IL, 60637
Ann Intern Med; 96(1):51-53 1982

We compared the utility of lower (30 mCi) and higher (50 to 60 mCi) doses of 131I, used to ablate residual thyroid tissue after thyroidectomy for carcinoma. Whole body scans were done using 1 mCi 131I, 3 wk after withdrawal of triiodothyronine. Patients had received ablation therapy within 3 days after scanning, and one or more subsequent scans were analyzed. Forty-eight patients were treated to ablate residual thyroid tissue that was presumed to be normal. Among 18 patients given the lower dose of 131I as outpatients, 15 had s[illegible] ablation and three needed a second administration; a[illegible] tients treated with the higher dose had successful abla[illegible] enteen additional patients, presumed to have residua[illegible] received 50 to 150 mCi; and six needed treatment. [illegible] one dose of 50 to 60 mCi 131I provides more certain [illegible] use of the usually effective 30-mCi dose for initial a[illegible] justified by the convenience of outpatient administr[illegible] lower expense, and the lower whole-body radiati[illegible] (Author abstract) (12 Refs)

22. EFFECTIVE FOCAL DOSAGE AND RADIATION LOAD DURING TREATMENT OF THYROID CANCER WITH IODINE RADIOISOTOPE.

Ivanitskaia VI, Shantyr' VI, Pudovkina LF, Kozhukhov VD
Res. Inst. Medical Radiology, Kharkov, USSR
Med Radiol (Mosk); 26(11):6-12 1981

To determine the effective doses of 131I for the treatment of thyroid cancer, 305 patients were reviewed. Tumor regression of 5-15 yr duration was achieved in 140/305 patients (22 men, 118 women; 19-73 yr old). Of 140 patients, 53 were in Stage II, 71 were in Stage III, and 16 were in Stage IV. The patients received 131I in combination with thyroidectomy or distant gamma therapy. Absorbed doses of 131I in the primary tumor and in lung metastases were 11,970 and 12,980 rads, respectively. Regression of lung metastases was observed in 26.5% of the patients treated with 131I after surgical removal of the thyroid, compared with 13.4% of the patients treated with 131I in combination with thyroid irradiation. Large lung metastases were more resistant to 131I than small disseminated lung metastases. The patients treated with 131I showed no impairment of liver and kidney functions. (16 Refs) (In RUS)

23. SUPPRESSIVE THERAPY FOR RADIATION-ASSOCIATED NODULAR THYROID DISEASE: DOUBLE-BLIND STUDY WITH T3 AND DESICCATED THYROID.

Tamura K, Shimaoka K, Tsukada Y, Razack MS, Sciasicia [illegible]
Dept. Medicine, Miyazaki Medical Coll., Kiyotake, Miya[illegible] Japan
Jpn J Clin Oncol; 11(3):457-462 1981

Suppressive therapy with either triiodothyronine (T3, 50 mg/day) on desiccated thyroid (DT, 120 mg/day) were carried out in a double blind study in 250 patients over a period of 6 mo. The patients had received radiation therapy (estimated av 400 rads) for various 27 yr before conditions at [illegible] av of 27 yr (11-52 yr) before thyroid abnormalities were detected in routine screening; many had exhibited pretreatment thyroid abnormalities of various kinds. Responses to therapy were as follows: complete response (T3, 37/124; DT, 35/126), partial response (T3 27/124; DT 34/126), improvement (T3, 17/124; DT, 16/126), and no change or progression (T3, 4[illegible]/124; DT 41/126). Thyroid scan did not show differences that agreed with responses. Thyroidectomy was performed on [illegible]8 patients who had not shown nodule disappearance after 6 mo. Predominant pathologic diagnoses were:carcinoma (11), chronic thyroiditis (26), adenoma (6), colloid nodule (7), and others (8). The results show the value of a screening program for high-risk patients. (22 Refs)

24. SQUAMOUS CELL CARCINOMA OF THE THYROID GLAND: TRANSITION FROM [illegible] CARCINOMA.

[illegible]

In eight autopsy cases of thyroid carcinoma, adenocarcinoma and squamous cell carcinoma coexisted, and presented. In these adenosquamous cell carcinoma, pathological findings suggest direct transition from papillary adenocarcinoma to squamous cell carcinoma, rather than transformation to squamous cell carcinoma via squamous metaplasia. We believe that squamous cell carcinoma arises from adenocarcinoma of the thyroid in most cases. (Author abstract) (24 Refs)

25. SERUM AND URINE CALCITONIN LEVELS IN PATIENTS WITH MEDULLARY THYROID CARCINOMA AND WITH NON-THYROIDAL CANCER AND THEIR IMMUNOLOGICAL SIZE-HETEROGENEITY.

Morimoto S, Onishi T, Imanaka S, Kumahara Y, Okada Y, Takai S, Miyauchi A, Nishioka Y
Dept. Medicine and Geriatrics, Osaka Univ. Medical Sch., Fukushima-ku, Osaka, Japan
Nippon Naibunpi Gakkai Zasshi; 57(8):1127-1138 1981

Levels of human calcitonin (hCT) were measured in serum and urine samples from 66 normal subjects (35 men, 31 women; 18-45 yr old), 24 patients with medullary thyroid carcinoma (MTC), and 277 patients with non-thyroid malignant tumors (NTMT). Serum samples were obtained from patients in the morning prior to eating and were centrifuged within 2 hr of sampling. Levels of serum hCT were determined with the aid of radioimmunoassay (RIA). Levels of urinary hCT were measured with RIA after the urine samples were boiled for 2 min, mixed with blue dextran, and passed through a Bio-Gel column. [illegible] known types of cancer). Levels of urinary hCT were 66-270 pg/mg creatinine (CR) in 56/66 normal subjects, 1.7-526 ng/mg CR in 11/24 patients with MTC, and 60-83,000 pg/mg CR in 82/277 patients with NTMT. Levels of urinary hCT were 3.4-20.8x higher than levels of serum hCT in 11/24 patients with MTC. Four distinct forms of immunoreactive calcitonin (IC) were observed in serum samples from three patients with MTC, and one main form of IC was observed in a urine sample from a patient with oat cell carcinoma of the lung. Measurement of serum and urinary hCT levels was thought to be useful for detecting cases of MTC and ectopic calcitonin-secreting tumors. (29 Refs) (In JPN)

26. THE PROGNOSTIC AND BIOLOGICAL SIGNIFICANCE OF CELLULAR HETEROGENEITY IN MEDULLARY THYROID CARCINOMA: A STUDY OF CALCITONIN, L-DOPA DECARBOXYLASE, AND HISTAMINASE.

[illegible]
[illegible]
[illegible]

We evaluated the cellular distribution of calcitonin (CT), L-dopa decarboxylase (DDC), and histaminase (diamine oxidase (DAO)) in 31 patients with medullary thyroid carcinoma (MTC). CT immunostaining was uniform (greater than 90% of the cells) and intense (4+) in lesions from seven patients with C-cell hyperplasia and six with microscopic MTC; conversely, patchy CT staining (less than 40% of the cells) and diminished intensity (1+) were found in metastases from eight patients who died of virulent disease. In 17 patients who underwent thyroidectomy for macroscopic cervical MTC with no evident distant metastases, CT staining was intense (3-4+) and homogeneous (greater than 90%) in 11 subjects who were well 0.5-16 yr postoperatively. Six patients with similar clinical presentations had heterogeneous staining for CT in primary tumor (less than 40% of the cells; 1-2+ intensity); five died of disseminated MTC 0.5-5 yr postoperatively (p less than 0.001). Biochemical studies of distant metastases revealed an inverse relationship between the distribution of CT and that of both DDC (r = -0.71; p less than 0.01) and DAO (r = -0.81; p less than 0.001). We conclude that cellular heterogeneity in MTC tissue is associated with a distinct biochemical pattern, and its presence, whether in a primary or metastatic lesion, indicates a virulent neoplasm associated with a grave prognosis. (Author abstract) (34 Refs)

PARATHYROID TUMORS

27. PARATHYRIN (PARATHYROID HORMONE): RADIOIMMUNOASSAYS FOR INTACT AND CARBOXYL-TERMINAL MOIETIES.

[illegible]
[illegible]
[illegible]

Radioimmunoassay (RIA) procedures for measurement of intact or carboxy (C-terminal) parathyrin (parathyroid hormone; PTH) in blood are described in detail. Clinical applications of the assays are discussed. Both RIAs use the same bovine PTH for standards and radioiodination, the same dextran-coated charcoal preparation (for separation of antibody-bound and free 125I-labeled PTH), and the same types of equipment. The major difference between the assays is that the antiserum against intact PTH was produced in a guinea pig immunized with bovine PTH conjugated to bovine serum albumin; the antiserum against C-terminal PTH was produced in a guinea pig immunized with a human C-terminal PTH fragment. The two PTH assays have achieved a consistent record of performance, reliability, and clinical usefulness. Applications of the assays include the diagnostic evaluation of patients with hypercalcemia, hypocalcemia, or chronic renal failure and preoperative venous catheterization to localize hyperfunctioning parathyroid tissue. Causes of hypercalcemia identified by PTH measurements include parathyroid adenomas, ectopic PTH secretion by nonthyroid cancers, and malignant tumors that do not produce immunoreactive PTH. (35 Refs)

28. DEVELOPMENT AND VALIDATION OF A NEW RADIOIMMUNOASSAY FOR PARATHYRIN (PTH).

[illegible]
Mayo Clinic and Mayo Foundation, Rochester, MN [illegible]
[illegible]

A radioimmunoassay for human parathyrin has been developed and characterized with whole-molecule (residues 1-84) human parathyrin and with the 1-34, 44-68, and 53-84 amino acid residue fragments of it. The antiserum used reacted with the whole molecule and with the 44-68 and 53-84 fragments but not with the 1-34 fragment. Parathyrin concentrations in the serum of 110 normal subjects and of 112 patients with surgically proved primary hyperparathyroidism were determined with this assay. The mean results were 39 (SD 13) µl-Eq/mL for the normals and 111 (SD 77) µl-Eq/mL for the patients with primary hyperparathyroidism (p less than 0.0005). The upper 95% confidence limit of the normal range was 60 µl-Eq/mL. For 54 patients with primary hyperparathyroidism, the preoperative values for serum parathyrin, calcium, and phosphate-but not creatinine-were statistically different from the postoperative values (paired t-test, p less than 0.0005). Normal subjects showed significant (p less than 0.0005) differences in serum calcium concentrations but not in parathyrin concentrations, compared with concentrations found in cancer patients and patients who had thiazide-induced hypercalcemia. Phosphate concentration in serum, although not a specific indicator of disease, is a valuable clue to the diagnosis of primary hyperparathyroidism. (Author abstract) (17 Refs)

ADRENAL TUMORS

29. LOCALIZATION OF FUNCTIONAL ADRENAL TUMORS BY COMPUTED TOMOGRAPHY AND VENOUS SAMPLING.

[illegible]
[illegible]
Radiology; [illegible]

Fifty-eight patients with functional lesions of the adrenal gland underwent radiographic evaluation. Twenty-eight patients had primary aldosteronism (Conn syndrome), 20 had Cushing syndrome, and 10 had pheochromocytoma. Computed tomography (CT) correctly identified adrenal tumors in 11 (61%) of 18 patients with aldosteronomas, 6 of 6 patients with benign cortisol-producing adrenal tumors, and 5 (83%) of 6 patients with pheochromocytomas. No false-positive diagnoses were encountered among patients with adrenal adenomas. Bilateral adrenal hyperplasia appeared on CT scans as normal or prominent adrenal glands with a normal configuration; however, CT was not able to exclude the presence of small adenomas. Adrenal venous sampling was correct in each case, and reliably distinguished adrenal tumors from hyperplasia. Recurrent pheochromocytomas were the most difficult to localize on CT due to the surgical changes in the region of the adrenals and the frequent extra-adrenal locations. (Author abstract) (22 Refs)

30. PREOPERATIVE LOCALIZATION OF ALDOSTERONE-SECRETING ADRENAL ADENOMAS.

[illegible]

Techniques for preoperative localization of aldosterone-secreting adrenal adenomas were studied in [illegible] patients, each with hypertension and biochemical evidence of primary hyperaldosteronism and each later having adrenal surgery ([illegible] adenomas, [illegible] bilateral adrenal hyperplasia). Bilateral adrenal vein catheterization was attempted in all cases; it was successful on the left side in all patients and in 92% of cases on the right. Adrenal vein plasma samples were obtained from the left side in 92% and from the right in 73% of cases. Adrenal vein plasma aldosterone measurements correctly indicated the presence of tumor in [illegible] cases but falsely predicted unilateral adenoma in two cases of bilateral adrenal hyperplasia. Adrenal venography also correctly predicted unilateral adrenal adenomas in 26 cases but falsely suggested the presence of tumor in 3 cases of bilateral adrenal hyperplasia. Computed tomography (CT) was used in the last eight cases. In seven instances the predictions (6 adenomas, 1 bilateral adrenal hyperplasia) were confirmed at surgery. However, the remaining patient harbored an adenoma 20 mm in diameter which was not detected by CT although diagnosed both by adrenal venography and adrenal vein aldosterone measurements. Ultrasound detected adenoma in only 3 of 22 cases examined. Although further comparative studies of the type described here are required, the results of computed tomography are promising and suggest that this non-invasive technique might well become the first choice procedure in localizing aldosterone-secreting adenomas. (Author abstract) (41 Refs)

31. ULTRASTRUCTURE OF ALDOSTERONE SECRETING ADRENAL ADENOMATA.

[illegible]

Two adrenocortical adenomas causing Conn's syndrome were examined by electron microscopy. Adenomatous cells were arranged in small clusters and showed a rather different morphology, especially as far as mitochondria were concerned. Some cells contained mitochondria with lamellar and tubular cristae (zona glomerulosa-like cells), while other parenchymal elements displayed mitochondria with tubular and vesicular cristae (zona fasciculata-like cells). Both cell types were endowed with a quite well developed smooth endoplasmic reticulum, some lipid droplets and a prominent Golgi apparatus. Moreover, adenomatous cells with large masses of lipofuscin pigment granules were also observed (zona reticularis-like cells). These findings stress the structural heterogeneity of the Conn's adenomata. (Author abstract) (21 Refs)

32. POSTOPERATIVE COURSE OF PRIMARY ALDOSTERONISM.

Tenschert W, Klaiber E, Luscher T, Greminger P, Tuma J, Reutter F, Wiher H, Havelka J, Siegenthaler W, Vetter H, Vetter W
(c/o W. Vetter) Departement fur Innere Medizin, Universitatsspital, CH-8091 Zurich, Switzerland
Schweiz Med Wochenschr; 112(3):86-90 1982

The effect of unilateral adrenalectomy was investigated in 15 patients with aldosterone producing adenoma and in 7 patients with bilateral adrenal hyperplasia. Mean postoperative observation period was comparable in both groups [illegible]. Preoperatively, mean blood pressure values in adenoma were [illegible] mm Hg and in hyperplasia [illegible] mm Hg. [illegible] After unilateral adrenalectomy the blood pressure values in patients with adenoma were reduced to [illegible] mm Hg and in those with bilateral hyperplasia to [illegible] mm Hg. In cases with adenoma a slight increase in plasma renin activity ([illegible] ng/ml 3 hr) and relatively low plasma aldosterone levels ([illegible] pg/ml) were observed. Mean postoperative serum potassium concentration in this group of patients was 4.0 ± 0.2 mval/l. In patients with hyperplasia the corresponding values for PRA were 2.7 ± 3.9 ng/ml 3 hr and for serum potassium 3.8 ± 0.3 mval/l, whereas plasma aldosterone levels increased to values of [illegible] ± 135 pg/ml. Ten of the 15 patients with adenoma (67%) were cured postoperatively and 5 cases (33%) showed normal blood pressure values under antihypertensive treatment. On the other hand, in the group of patients with bilateral hyperplasia only one of the seven cases (14%) was cured postoperatively, whereas in four cases (57%) normal blood pressure values were achieved under antihypertensive treatment. In two patients (29%) blood pressure was not reduced under antihypertensive treatment. The results show that unilateral adrenalectomy has a favorable effect in patients with an aldosterone producing adenoma, whereas cases with bilateral adrenal hyperplasia show only slight response to surgical treatment. (Author abstract) (10 Ref.) (In GER)

33. PRESERVATION OF ADRENOCORTICAL FUNCTION DURING SURGERY FOR BILATERAL PHEOCHROMOCYTOMA.

[illegible]
Dept. Endocrinology, Englewood Hosp., Englewood, NJ
J Urol; [illegible] 1982

A case is reported of bilateral pheochromocytoma treated by bilateral adrenalectomy. A portion of the left adrenal cortex was left in the adrenal bed, although the arterial and venous blood supply had been ligated. A successful autograft was documented [illegible] postoperatively. A review of the literature failed to reveal any such successful attempt in the management of bilateral pheochromocytoma. The patient has a normally functioning adrenal cortex that responds to adrenocorticotropic hormone stimulation in the usual manner. The procedure is recommended in cases of bilateral pheochromocytoma because of its apparent ease and because it obviates the need for a lifetime of adrenocortical steroid replacement. (Author abstract) (11 Refs)

34. BLOOD LEVELS OF O,P'-DDD FOLLOWING ADMINISTRATION IN VARIOUS VEHICLES AFTER A SINGLE DOSE AND DURING LONG-TERM TREATMENT.

Moolenaar AJ, Van Slooten H, Van Seters AP, Smeenk D
Diaconessenhuis, (c/o van Slooten) Houtlaan 55, 2334 CK Leiden, The Netherlands
Cancer Chemother Pharmacol; 7(1):51-54 1981

Plasma levels (PL) of 2,2-bis(2-chlorophenyl,4'-chlorophenyl)1,1 dichloroethane (o,p'-DDD) were measured in patients being treated for adrenocortical cancer (ACC) or pituitary-dependent Cushing's syndrome. Measurements were made in plasma of 19 patients after single doses of 2g: Nine patients received commercially available tablets (Tab), 12 received en-

[illegible] Tab produced lower levels; Gra produced the lowest PL. Nausea and borborygmus were reported with Gra but not with other vehicles. PL after long-term administration were higher for Mlk than for Eml but not significantly so; Tab produced significantly lower PL. Recovery of o,p'-DDD from feces was 40% with Tab and less than 10% with Eml or Mlk. Therapy with 4-10 g o,p'-DDD/day in 3-4 equal doses administered as Mlk is recommended, with frequency and daily dose adjusted when PL exceeds 20 ug/ml. (14 Refs)

PANCREAS TUMORS

35. ANGIOGRAPHY IN DIAGNOSIS OF PANCREATIC INSULINOMAS.

Markov IN, Privezentseva TV
First Dept. Surgery, Central Inst. Advanced Training for Physicians, Moscow, USSR
Khirurgiia (Mosk); (11):6-10 1981

Diagnostic efficacy of angiography was evaluated in 16 patients (4 men, 12 women; 26-57 yr old) with hypoglycemia. Angiographic signs of pancreatic insulinoma were observed in 13/16 patients. Characteristic angiographic findings included hypervascularization, presence of dense network of small convoluted vessels during the arterial phase, and presence of round homogenous shadow during the capillary and late venous phases. In one patient, angiography showed liver metastases of malignant insulinoma. Of [illegible] patients subjected to surgery, [illegible] were found to have insulinomas in the [illegible] of the head of the pancreas and [illegible] had tumors located between the body and the tail of the pancreas. False positive angiographic findings were associated with contrasting of the left adrenal or with inflammation of the pancreas during penetration of the duodenal ulcer. (26 Refs) (In RUS)

36. LOCALIZATION OF ISLET CELL TUMORS USING SONOGRAPHY, COMPUTED TOMOGRAPHY, ARTERIOGRAPHY AND SELECTIVE TRANSHEPATIC VENOUS SAMPLING FOR HORMONE ASSAY.

Gunther R, Kummerle F, Beyer J, Klose K, Kuhn FP, Ruckert K, Cordes U
Institut fur klinische Strahlenkunde, Universitat Mainz, Langenbeckstr. 1, D-6500 Mainz, W. Germany
ROEFO; 135(6):657-662 1981

Of 29 patients examined operation revealed a malignant tumor in 9 and a benign insulinoma in 18; 2 insulinomas were not found. The problems of preoperative tumor localization were limited to small insulinomas (size 7-35 mm). Ultrasound detected all of three insulinomas as low echogenic structures (size 7, 8, 17 mm). Computed tomography demonstrated four of five insulinomas (size 7, 8, 15, 17 mm) due to contrast enhancement following bolus injection. Arteriography localized 12 of 18 insulinomas preoperatively and 14 of 18 retrospectively. Selective transhepatic venous sampling for insulin assay [illegible] (Author abstract) (17 Refs) (In GER)

37. LOCATION OF AN INSULINOMA BY TRANSHEPATIC PHLEBOGRAPHY WITH STAGED INSULIN ASSAYS.

Dupuy J, Frija G, Baccari F, Girardot P, Frisson J, Franc B, Basic E, Colliard M
Polyclinique, Hopital Ambroise Pare, 9, av Charles De Gaulle, F 92100 Boulogne, France
Nouv Presse Med; 10(45):3711-3714 1981

Insulinoma was easily diagnosed in a 73-yr-old woman who had organic hypoglycemia associated with hyperinsulinism, but the tumor could not be located by echotomography and computerized tomography. The state of the patient's arteries precluded arteriography. Pancreatic phlebography was carried out by the portal transhepatic route and blood was collected at different levels for plasma insulin assays. A very high gradient at the pancreatic isthmus indicated the site of the tumor, which was found on surgery to be precisely there and could be enucleated. The technique cannot be used systematically to locate insulinomas, but it is unquestionably helpful when the tumor cannot be located by other methods or when these are contraindicated. (Author abstract) (15 Refs) (In FRE)

38. INTRAOPERATIVE BIOCHEMICAL LOCALIZATION OF INSULINOMA BY QUICK RADIOIMMUNOASSAY.

Teichmann RK, Spelsberg F, Heberer G
Dept. Surgery, Univ. Munich, Klinikum Grosshadern, Marchioninistrasse 15, 8000 Munich 70, W. Germany
Am J Surg; 143(1):113-115 1982

In patients with organic hyperinsulinism, intraoperative determination of insulin concentrations in veins draining the pancreas might help localize the tumor. We have developed a radioimmunoassay measuring insulin within 15 minutes. At operation, blood samples are taken at various sites in the splenic, superior mesenteric and portal veins for insulin determinations. In all six patients, the highest insulin concentrations correlated with the site of the tumor. Also, small insulinomas less than 1 cm in diameter could be found. In one patient the tumor appeared to secrete mainly proinsulin. By this procedure we hope to avoid blind distal resection of the pancreas and possibly invasive preoperative diagnostic procedures. (Author abstract) (7 Refs)

39. PANCREATIC SECRETING GLUCAGONOMA: CLINICAL, RADIOLOGICAL, HORMONAL, AND MORPHOLOGICAL STUDY; INHIBITORY EFFECT OF SOMATOSTATIN-14.

Vinel JP, Pradere B, Voigt JJ, Pradayrol L, Pascal JP
(c/o Pascal) Service d'Hepato-Gastroenterologie, C.H.U., F-31059 Toulouse-Purpan, France
Gastroenterol Clin Biol; 5(12):1155-1159 1981

The nature of the hormonal products secreted, the mode of secretion, and the biological diagnosis of a secreting pancreatic glucagonoma as found in a 52-yr-old woman are described. The patient presented with skin eruptions, wt loss, glossitis, balanitis, and a recent development of diabetes. Arteriography and glucagon measurement in the portal area allowed tumor localization, and detection of the hyperglucagonomia. A caudal spleno-pancreatectomy was performed. Anatomopathological characteristics of the glucagonoma are described. (23 Refs) (In FRE)

40. GLUCAGONOMA TUMORS AND SYNDROME.

Montenegro-Rhodas F, Samaan NA
No affiliation given
Curr Probl Cancer; 6(6):1-54 1981

The pathobiology of glucagonoma tumors and the glucagonoma syndrome are described in detail. Every tumor of the alpha (a)-cells of the pancreas can be considered a glucagonoma. Glucagonoma can found as a tumor only, as glucagonoma tumor in other pancreatic syndromes, and glucagonoma syndrome. Findings in 10 patients with glucagonoma tumor only, 12 patients with glucagonoma tumor in other pancreatic syndromes, and 77 patients with glucagonoma syndrome are presented. Glucagonoma syndrome is characterized by secondary diabetes mellitus, necrolytic migratory erythema, weight loss, and anemia. Erythematous nodular lesions are sometimes seen in patients with acinar cell pancreatic carcinoma. All patients who have glucagonoma syndrome have a glucagon-secreting a-cell tumor of the pancreatic islets. The tail of the pancreas is the most frequent site of tumor, but they can be found in any region of the pancreas. Most tumors have metastasized at the time of diagnosis. The absence or presence of metastases cannot be predicted by plasma glucagon levels, or by size of the tumor. Local lymph nodes and liver seem to be the most frequent sites of metastatic involvement. Glucagonoma syndrome should be suspected in patients who have diabetes mellitus and significant weight loss in spite of satisfactory control of diabetes. Surgery is the treatment of choice, and clinical improvement is often dramatic, though short-lived. The longest disease-free interval reported in a patient without metastases has been 4 yr. Chemotherapy may induce a temporary remission, and various treatment regimens have been tried on very small numbers of patients. Patients treated with chemotherapy live at least as long as the mean of all treated patients, and may live slightly longer than those untreated. (136 Refs)

GONADAL TUMORS

41. COMMERCIAL RADIOIMMUNOASSAY FOR BETA SUBUNIT OF HUMAN CHORIONIC GONADOTROPIN: FALSELY POSITIVE DETERMINATIONS DUE TO ELEVATED SERUM LUTEINIZING HORMONE.

Fowler JE, Platoff GE, Kubrock CA, Stutzman RE
Univ. Virginia Sch. Medicine, Charlottesville, VA, 22908
Cancer; 49(1):136-139 1982

Among 17 men who had received seemingly curative treatment for unilateral non-seminomatous germ cell tumors for the testis and who had consistently normal serum human chorionic gonadotropin (HCG) levels at a reference laboratory, 7 (41%) had at least one falsely positive commercial serum HCG determination. To investigate the cause of these falsely positive determinations the authors measured the cross reactivity of luteinizing hormone (LH) and follicle stimulating hormone (FSH) standards in the commercial HCG assay, and studied the relationships between commercial HCG levels and serum LH levels, serum FSH levels and gonadal status in men with and without normal gonadal function. The falsely positive HCG determinations appeared to be due to elevated serum LH levels and cross reactivity of LH in the commercial HCG assay because: (1) there was substantial cross reactivity of the LH standards in the commercial assay, (2) the serum LH was elevated in four of six men with solitary testes, (3) there was a striking correlation between elevated serum LH levels and falsely elevated commercial HCG levels in 10 men with solitary or absent testes, and (4) there were no falsely positive HCG determinations in 13 normal men but there were falsely positive HCG determinations in 7 of 10 anorchid men. (Author abstract) (8 Refs)

42. CELLULAR LOCALIZATION OF AFP, HCG AND ITS FREE SUBUNITS, AND SP1 IN EMBRYONAL CARCINOMA OF THE TESTIS AND OVARY.

Furumoto M
Dept. Pathology, Kobe Univ., Sch. Medicine, 5,7-Chome, Kusunoki-Cho, Chuoku, Kobe, Japan
Pathol Res Pract; 173(1/2):12-21 1981

An immunohistologic study of AFP, hCG and its free subunits, and SP1 was investigated in 10 cases of non-seminomatous germ cell tumors of the testis and ovary. AFP was demonstrated in mononuclear embryonal tumor cells within embryonal carcinoma in a narrow sense, frequently in association with yolk sac tumor. AFP was more consistently demonstrated in vacuolated or elongated cells of yolk sac tumor, in which continuous transformation from tubular patterns of embryonal carcinoma was shown with positive reactions from AFP. The hCG was demonstrated in syncytiotrophoblastic giant cells scattered among the embryonal carcinoma, but rarely in mononuclear large cells. The occurrence of hCG and beta subunit was more frequently observed than alpha subunit or SP1, suggesting the unbalanced synthesis of hCG and free subunit in choriocarcinomatous element associated with embryonal carcinoma. These findings support the view that embryonal carcinoma has a developmental potential to the extra-embryonic components of both choriocarcinoma and yolk sac tumor. (Author abstract) (29 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

43. PREDICTING TREATMENT RESPONSE IN BREAST CANCER USING URINARY DISCRIMINANT RATIO AND RECEPTOR ASSAY.

Holdaway IM, Skinner SJ
Dept. Endocrinology, Auckland Hosp., Auckland 1, New Zealand
Eur J Cancer Clin Oncol; 17(12):1295-1300 1981

The ratio of urinary 11-desoxy-17-oxo steroids to urinary corticosteroids (discriminant ratio, DR) was compared with levels of tumor estrogen (ER) and progesterone (PR) receptor in 16 9 patients with early breast cancer. Approximately 205 of patients had significant levels in all three tests and 20% were negative by all three assays. However, patient status by ER and DR assay was in disagreement in 50% of cases. Retrospective analysis of 78 treatment courses of endocrine therapy in patients with disseminated breast cancer showed that out of the three predictive tests only ER assays reliably distinguished responding from non-responding patients. The same result was observed in a subgroup of 20 patients undergoing adrenal suppression with aminoglutethimide. When tests were combined in pairs, no combination, including either ER and PR or ER and

DR, showed improved discrimination between responding and nonresponding patients compared to that seen with ER alone. No predictive assay or combination of assays could usefully distinguish patients with a high likelihood of response to endocrine therapy. (Author abstract) (13 Refs)

44. TURISTERON: CLINICAL EXPERIENCE WITH A DEPOT ESTROGEN IN THE TREATMENT OF METASTATIC MAMMARY CARCINOMA.

Gurtler R, Tannenberger S, Bodek B, Morack G, Tannenberger S, Bodek B, Morack G
Zentralinstitut fur Krebsforschung der AdW, Lindenberger Weg 80, DDR-115 Berlin-Buch, E. Germany
Arch Geschwulstforsch; 52(2):129-139 1982

Sixty patients (54-86 yr old, av age 70 yr) in late menopause with metastatic mammary carcinoma were treated with the depot estrogen Turisteron. Forty-nine patients had undergone radical mastectomy; 2 had undergone simple mastectomy. Results in 51/60 patients were evaluable. Of these 51, 11 received 1 mg Turisteron/wk, po; 40 received 2 mg/wk. The lower dose was found to be unsatisfactory; a dose of 3 mg/wk was not tolerated well. Of the 40 patients receiving 2 mg/wk, 7.5% achieved complete remission with an av duration of 27 mo; 22.5% achieved partial remission with a 10 mo av duration, 10.0% showed clinical improvement, 32.5% showed tumor progress, 5.0% showed tumor stimulation, and 5.0% showed hypercalcemia. Results of therapy began to appear 4-6 wk after start of treatment. Turisteron was particularly effective against soft-tissue and lung metastases. Results indicate that Turisteron is suitable for treatment of metastatic mammary carcinoma during late menopause. Contraindications for treatment include cardiovascular disorders, liver damage, and hypercalcemia. Replacement of Turisteron therapy with cytostatic therapy if tumor stimulation occurs is recommended. (26 Refs) (In GER)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

45. THE EFFECTS OF HODGKIN'S DISEASE AND COMBINATION CHEMOTHERAPY ON GONADAL FUNCTION IN THE ADULT MALE.

Whitehead E, Shalet SM, Blackledge G, Todd I, Crowther D, Beardwell CG
(c/o Shalet) Dept. Endocrinology, Christie Hosp., Wilmslow Road, Manchester M20 0BX, England
Cancer; 49(3):418-422 1982

The effects of Hodgkin's disease and quadruple chemotherapy on gonadal function have been investigated in 93 male patients with Hodgkin's disease. Nineteen men were studied before they received chemotherapy. Fifteen of the 19 had a sperm count of 20 million/ml or greater and motility was at least 40% in all 15. In the remaining 74 men, gonadal function was studied after completion of chemotherapy (6 mo-8 yr). Semen was obtained from 49 men who had received six or more courses of MVPP. Forty-two were azoospermic and 5 of the remaining 7 had a sperm count below 1 million/ml. Decreased libido and sexual activity was common during treatment but in the majority of men these returned to normal after completion of chemotherapy. The median FSH and LH levels and the median increments in semen FSH and LH levels after LHRH administration were significantly elevated compared with an age-matched control group. The mean testosterone level of the patients was significantly lower than in controls suggesting Leydig cell damage but androgen replacement therapy was not indicated in any individual patient. No evidence of hyperprolactinemia as a result of MVPP therapy was found. These results suggest that sperm storage before chemotherapy represents the main possibility for these patients to have children after completing chemotherapy. Before starting chemotherapy, advice should be given to these patients concerning possible changes in sexual behavior during treatment and the very high incidence of permanent infertility following treatment. (Author abstract) (21 Refs)

46. HODGKIN'S DISEASE IN CHILDREN: LONG-TERM THERAPEUTIC RESULTS.

Cramer P, Schaison G, Andrieu JM, Boiron M, Bernard J
Institut de Recherche sur les Leucemies et les Maladies du Sang, Hopital Saint-Louis, 2, place du Docteur-Fournier, F-75475 Paris Cedex 10, France
Bull Cancer (Paris); 68(5):456-464 1981

Between 1965 and 1976, 83 previously untreated children aged 15 yr and under, with biopsy-confirmed Hodgkin's disease were assessed, treated, and followed-up at the Hospital Saint-Louis, in Paris. Clinical stages were IA-IIA for 59, IB-IIB for 19, and III-IV for 5 patients. Two main types of treatment were used: monochemotherapy-radiotherapy in 26 patients who received mantle field irradiation followed by monthly vinblastine injections for 3 yr; 57 patients received a combination of MOPP and radiotherapy. The MOPP-radiotherapy treated patients have a significantly better survival and relapse-free survival than the monochemotherapy-radiotherapy treated patients (86.9% vs 76.1% and 83.5% vs 65.4%). Thirteen relapses were observed after a median complete remission period of 30 mo: 6 patients are now free from disease and 1 is still under treatment. Ten patients died after a 55 mo median survival: 7 died from Hodgkin's disease and 3 from treatment toxicity. No secondary cancer or leukemia has been observed. The main long-term complications of therapy were sterility in male patients, after chemotherapy, and growth defects and disturbances of thyroid functions after radiotherapy. (Author abstract) (47 Refs) (In FRE)

47. A STUDY OF PROSTAGLANDIN E2, PARATHORMONE, AND RESPONSE TO INDOMETHACIN IN PATIENTS WITH HYPERCALCEMIA OF MALIGNANCY.

Brenner DE, Harvary HA, Lipton A, D[illegible]rs L
Div. Oncology, Dept. Medicine, Vanderbilt Univ., A2127 MCN, Nashville, TN, 37232
Cancer; 49(3):556-561 1982

In order to evaluate the relationship of PGE2 to hypercalcemia in cancer patients, 101 patients were screened with a radioimmunoassay for plasma prostaglandin E2 (PGE2) (NL less than 100 pg/ml). Of the 101 patients, 31 were hypercalcemic. Mean PGE2 (+- SEM) of the 31 patients was 199 +-36 pg/ml. Among the 70 normocalcemic patients, mean +- SEM PGE2 was 85 +-12 pg/ml (range = less than 25-225 pg/ml) (p less than 0.001). Seventeen hypercalcemia patients were initially treated with saline and furosemide, then were prospectively screened for serum parathormone (iPTH) and PGE2. Fourteen of 17 patients were then treated empirically with indomethacin (25 mg bid) for 72 hours and the PGE2 assav was repeated. Prior to therapy with indomethacin (mean +- SEM), CA + + = 12.2 + 1.5 mg/dl (NL 8.4-10.6 mg/dl), PGE2 = 87.1 +- 36.8 pg/ml, (range = less than 25-209 pg/ml), and iPTH =

406 +-266 pg/ml (NL less than 400 pg/ml) (range = less than 100-825 pg/ml). PGE2 was elevated before treatment in 6/14 patients (breast, colon, renal, lung, neck tumors, and myeloma). Following treatment with indomethacin, PGE2 and calcium fell to normal levels in three patients (breast, colon, renal carcinomas). These results suggest: (1) A bimodal distribution of PGEs exists in hypercalcemic cancer patients. (2) There was some evidence of lack of whole molecule iPTH suppression in these patients. (3) Multiple stimuli of calcium mobilization may play an important etiologic role in a few hypercalcemic cancer patients and may explain the failure of indomethacin to control serum Ca++ in some patients with elevated PGE2. (Author abstract) (44 Refs)

48. HYPERCALCEMIA IN CHRONIC MYELOID LEUKEMIA.

Weiss Z, Plato A, Cohen D
Dept. Internal Medicine, Valley Medical Center, Afula, Israel
Harefuah; 101(3):63-64,91 1981

Hypercalcemia is commonly associated with solid tumors of the breast, lungs, and kidneys. It occurs in only 2.5-4.5% of patients with leukemia, usually those with acute lymphocytic leukemia (ALL). It is exceedingly rare in chronic myeloid leukemia (CML). The case of a 67-yr-old man with a 5 yr history of CML (with positive Philadelphia chromosome) who presented with complaints of low back pain, weakness, and weight loss and was found to have hypercalcemia in the range 12-14 mg/deciliter is reported. The patient had a low normal parathyroid hormone level, normal thyroid function, and normal prostaglandin level. Bone x-rays and a bone scan were negative. The WBC count was in the range 15,000-30,000/cc; the patient was not undergoing a blast crisis. Despite symptomatic treatment with saline, diuretics, and steroids as well as chemotherapy with busulfan and hydroxyurea, the patient continued to manifest hypercalcemia and hyperphosphatemia. The various mechanisms of hypercalcemia in malignant disease are discussed; hypercalcemia in the patient was attributed to probable marrow invasion. No autopsy or bone marrow biopsy was available to confirm the hypothesis. (17 Refs) (In HEB)

49. COEXISTENT MULTIPLE MYELOMA AND PRIMARY HYPERPARATHYROIDISM.

Stone MJ, Lieberman ZH, Chakmakjian ZH, Matthews JL
Charles A. Sammons Cancer Center, Baylor Univ. Medical Center, 3500 Gaston Ave., Dallas, TX, 75246
JAMA; 247(6):823-824 1982

A patient with multiple myeloma and hypercalcemia responded to cytotoxic chemotherapy. However, hypercalcemia persisted. Because of the absence of lytic bone lesions, the presence of a low serum phosphate level, and a family history of possible primary hyperparathyroidism, the patient was evaluated for this disorder. Serum parathyroid hormone and urinary cyclic adenosine monophosphate levels were elevated. Exploration of the neck disclosed two enlarged parathyroid glands (1,850 mg and 210 mg), which were excised. After surgery, the patient's serum calcium levels remained normal for one year. Progressive myeloma bone disease developed that eventually resulted in recurrent hypercalcemia and death. Autopsy revealed only evidence of myeloma. (Author abstract) (9 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

50. BRONCHOGENIC CARCINOMA AND DIABETES INSIPIDUS: CASE REPORT AND REVIEW.

Krol TC, Wood WS
(c/o Wood) Community and Family Medicine, Loyola Univ. Stritch Sch. Medicine, 2160 South First Ave., Maywood, IL, 60153
Cancer; 49(3):596-599 1982

Tumor metastasis to the posterior pituitary-hypothalamic area rarely is expressed by either clinical or radiographic evidence. A case is reported of widespread metastatic ACTH secreting bronchogenic carcinoma presenting to the clinician as diabetes insipidus. This type of tumor associated with diabetes insipidus is apparently rare, as is antemortem radiographic documentation of metastasis to the pituitary-hypothalamic region. A review of the 10-year experience of Loyola University Medical Center and Hines VA Hospital with the association of bronchogenic carcinoma and diabetes insipidus is presented with a brief review of metastatic disease to the pituitary. (Author abstract) (20 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

51. ESTABLISHMENT OF FUNCTIONAL HUMAN PITUITARY TUMOR CELL CULTURES.

Melmed S, Odenheimer D, Carlson HE, Hershman JM
Endocrine Res. Lab., Medical and Res. Services, Wadsworth Veterans Admin. Medical Center, Los Angeles, CA
In Vitro; 18(1):35-42 1982

Five primary human pituitary tumor cell cultures were initiated from adenoma fragments obtained from patients with prolactin-secreting adenomas and acromegaly. Functional cell cultures were maintained and propagated in monolayer or suspension culture for up to 9 mo. Optimal cell viability and growth were achieved using Ham's F10 medium enriched with 20% fetal bovine serum, although cells from a patient with acromegaly also grew in serum-free, defined, hormone-containing medium. Bromocriptine (100 ng/ml) did not alter the growth curve of replicating cells derived from a patient with acromegaly. These cells initially secreted 5.5 ug human growth hormone/10(6) cells, and hormone production diminished after 6 wk. Prolactin secretion by cells derived from prolactinomas (0.5 to 1.3 ug/10(6) cells/24 hr) was stimulated by thyrotropin-releasing hormone (10 ng/ml) in two of the cultures. Both dopamine (10 ng/ml) and nickel chloride (1 mM) suppressed PRL secretion. These studies demonstrate that responsive human pituitary tumor cell cultures can be initiated and maintained. (Author abstract) (26 Refs)

52. HISTIDYL-PROLINE DIKETOPIPERAZINE SUPPRESSES PROLACTIN SECRETION IN HUMAN PITUITARY TUMOUR CELL CULTURES.

Melmed S, Carlson HE, Hershman JM
Dept. Medicine, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA
Clin Endocrinol (Oxf); 16(1):97-100 1982

Because histidyl-proline diketopiperazine (HPD), a metabolite of TRH, has been shown to suppress prolactin (PRL) release by rat pituitary tumor cells, human pituitary tumor cells were exposed to this compound. Monolayer cell cultures were initiated from pituitary tissue removed by transsphenoidal surgery from two patients with prolactin-secreting microadenomas. Tumor fragments were mechanically dispersed; cells were seeded into multiwell plates and incubated in Ham's F-10 medium enriched with fetal calf serum (20%). HPD (7.5 ng/ml) suppressed PRL release by both tumor cell cultures. Theophylline reversed the inhibition of PRL release induced by HPD. The data raise the possibility that HPD may act as an endogenous prolactin-inhibiting factor in man. (Author abstract) (7 Refs)

53. INDUCTION (OR STIMULATION) OF PROLACTIN AND GROWTH HORMONE PRODUCTION IN A RAT PITUITARY TUMOR CELL LINE BY BROMODEOXYURIDINE.

Cohen H, Andre J, Grenot C, Guillaumot P, Pascal O
Unite de Recherches Endocriniennes et Metabolliques, Chez l'Enfant, Hopital Debrousse, 29 rue Soeur Bouvier, 69322 Lyon Cedex 1, France
Endocrinology; 110(2):421-427 1982

Under basal conditions, a rat pituitary tumor cell line (C8 11RAP) does not secrete any detectable PRL, FSH, and LH, and secretes only minute amounts of GH (27.1 +-0.5 ng/10(6) cells/24 hr), as evaluated by RIA. Bromodeoxyuridine (BrdUrd) added to the culture medium induced the accumulation of PRL into cells and medium, increased that of GH, but did not induce that of LH or FSH. The amount of radioimmunoassayable PRL and GH accumulated in the medium increased after a lag period of 15 days and was drug concentration dependent. Maximal accumulation was 232.9 +-36.8 and 493.6 +-41.5 ng/10(6) cells/24 hr for PRL and GH, respectively, at 50 ug/ml BrdUrd. In the presence of BrdUrd (greater than or equal to 20 ug/ml), the cells grew more slowly and were more strongly attached to the flasks. All of the effects induced by BrdUrd were reversible. PRL and GH were characterized by three methods: (1) radiocompetition with increasing dilution of samples; (2) Sephadex chromatography, followed by RIAs; and (3) sodium dodecyl sulfate-polyacrylamide gel electrophoresis done on the immunoprecipitate of the proteins secreted by cells incubated with [3H]leucine. Chronic treatment with TRH (3 x 10(-6) M) of cells grown without BrdUrd was unable to increase the production of GH or to induce that of PRL. On the other hand, after the same treatment of cells cultured in the presence of BrdUrd, the amounts of PRL accumulated in the culture medium or cells were increased two- to seven-fold over unstimulated levels; under the same conditions, GH accumulation in the medium was also increased, but this augmentation was less than that of PRL. These results indicate that BrdUrd simultaneously induces or stimulates the production of PRL and GH in C8 11RAP cells, and that TRH increases the production of both hormones only in BrdUrd-treated cells. (Author abstract) (21 Refs)

54. REGULATION OF PITUITARY GROWTH AND PROLACTIN GENE EXPRESSION BY ESTROGEN.

Lieberman ME, Maurer RA, Claude P, Wiklund J, Wertz N, Gorski J
Dept. Biochemistry and Animal Science, Univ. Wisconsin, Madison, WI, 53706
Adv Exp Med Biol; 138:151-163 1982

The site of estrogen action and the molecular events involved in the regulation of prolactin synthesis were studied using monolayer cultures of dispersed rat pituitary cells. Primary cultures of rat pituitary cells respond to estradiol by increased incorporation of precursors into prolactin. Time and magnitude of response are in agreement with that observed under in vivo conditions suggesting that estrogen exerts its effect through a direct action on the pituitary gland. Chronic treatment with diethylstilbestrol caused sustained proliferation of pituitary tumors in the Fisher 344 rat, but not in the Holtzman rat. (33 Refs)

55. DEFECTIVE CENTRAL NERVOUS SYSTEM DOPAMINERGIC FUNCTION IN RATS WITH ESTROGEN-INDUCED PITUITARY TUMORS, AS ASSESSED BY PLASMA PROLACTIN CONCENTRATIONS.

Casanueva F, Cocchi D, Locatelli V, Flauto C, Zambotti F, Bestetti G, Rossi GL, Muller E
(c/o Muller) Dept. Pharmacology, Univ. Milan, Via Vanvitelli, 32, 20129 Milan, Italy
Endocrinology; 110(2):590-599 1982

Mature cycling female rats were each injected at 3-wk intervals with 2 mg estradiol valerate (EV) in sesame oil. Controls received an equivalent volume of sesame oil. The administration of EV induced, at first, hyperplasia and then, 10 wk after the first EV injection, adenomatous changes in the pituitary gland. Concurrently, there was a striking rise in plasma PRL concentrations, which reached values of about 2 ug/ml at 25 wk. Acute administration of nomifensine (NOM), an indirectly acting dopamine (DA) agonist, to EV-injected rats suppressed baseline PRL levels at 1 wk, but failed to significantly decrease PRL levels at 4, 7, 10, and 25 wk. Unlike NOM, bromocriptine, a direct DA agonist, strikingly reduced baseline PRL levels in EV-injected rats 1, 10, and 25 wk after the first EV injection. The administration of domperidone (DOM), a potent blocker of DA receptors, inconsistently increased plasma PRL at 1 wk and was ineffective at the following time intervals. Light and electron microscopic examinations of the hypothalamus revealed the existence in EV-injected rats of pathological changes in the arcuate nucleus region. In addition, measurement of DA in the median eminence of diluent- and EV-injected rats showed in the latter the presence of progressively reduced DA concentrations. These data suggest that rats with primary estrogen-induced PRL-secreting tumors have a defect in CNS-DA neurotransmission, a condition which has been postulated to also occur in human subjects bearing a prolactinoma. (43 Refs)

56. THE EFFECT OF RADIATION ON THYROID C CELLS.

Thurston V, Williams ED
Dept. Pathology, Welsh Natl. Sch. Medicine, Heath Park, Cardiff CF4 4XN, Wales
Acta Endocrinol (Copenh); 99(1):72-78 1982

To study the effects of radiation from 131I on thyroid C cells, newborn rats were given 0, 5 or 10 uCi 131I and studied at 3 monthly intervals over 2 yr. Routine stains, calcitonin immunolocalization and quantitation were used to study follicular and C cells. Both radiation doses led to almost complete disappearance of C cells, with only scattered morphological abnormal surviving cells. After a yr, some animals showed focal reappearance of C cells; these isolated clusters were interpreted as clones of cells, derived after a considerable lag period, from the very few surviving C cells which had not been sterilized. This focal regeneration was dose-dependent. It is concluded that C cells are much more radiosensitive to radiation from 131I than follicular cells. These observations support the use of

131I therapy in the treatment of post-operative thyroid residues in patients with C cell hyperplasia, or microscopic intrathyroid deposits of medullary carcinoma. (Author abstract) (11 Refs)

57. EVIDENCE FOR THE PRESENCE OF PRO-GAMMA-MELANOTROPIN, THE NH2-TERMINAL FRAGMENT OF THE CORTICOTROPIN-BETA-LIPOTROPIN PRECURSOR, IN CORTICOTROPIN-PRODUCING TUMOURS.

Alumets J, Ekman R, Hakanson R, Sundler F
(c/o Hakanson) Dept. Histology, Pharmacology and Nuclear Medicine, Univ. Lund, Solvegatan 10, S-223 62 Lund, Sweden
Virchows Arch [Pathol Anat]; 394(1/2):143-150 1981

Five corticotropin-producing tumors were examined for peptides related to the corticotropin-beta-lipotropin precursor. Two were basophil pituitary adenomas and three were bronchial carcinoids. The cells of the two pituitary adenomas stained with antisera against beta-endorphin and against pro-gamma-melanotropin, the NH2-terminal fragment of the corticotropin-beta-lipotropin precursor, but not with antisera against alpha-melanotropin or beta-lipotropin. The corticotropin-storing tumor cells of the bronchial carcinoids stained with antisera against beta-endorphin, beta-lipotropin or pro-gamma-melanotropin. Only one of the three bronchial carcinoids contained cells reacting with the antiserum against alpha-melanotropin. Although the two types of corticotropin-storing tumors (pituitary adenoma and bronchial carcinoid) differed with respect to beta-lipotropin content, the over-all picture indicates that the proteolytic processing of the corticotropin precursor proceeds along similar lines in tumor cells and in pituitary corticotrophs. An acetic acid extract of one of the bronchial tumors was subjected to gel chromatography and immunochemical analysis of material related to pro-gamma-melanotropin. The immunoreactive material displayed a considerable size heterogeneity, with the predominant components having a mol wt larger than that of authentic pro-gamma-melanotropin. (Author abstract) (21 Refs)

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. THE VALUE AND LIMITATION OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF INTRACRANIAL SPACE-OCCUPYING LESIONS.

Shen T, Chen S, Rong D, Chen G, Tang Z
Dept. Radiology, Huashan Hosp., Shanghai First Medical Coll., Shanghai, People's Republic of China
Zhonghua Fangshexue Zazhi; 15(2):87-90 1981

Computed tomography (CT) diagnosis of intracranial space-occupying lesions is described. The 236 cases examined in this series included gliomas (65 cases), pituitary adenomas (41 case s), meningiomas (30 cases), acoustic neuromas (19 cases), craniopharyngiomas (14 cases), pinealomas (7 cases), metastatic tumors (4 cases), angioblastomas (3 cases), myeloblastomas (2 cases), microgliosarcomas (2 cases), intracranial hematomas (27 cases), and others. Results showed that CT was valuable in accurately locating intracranial space-occupying lesions but it was much less useful in correctly diagnosing the nature of the lesions. However, due to the fact that most of these lesions often exhibit typical features, correct diagnosis was still achieved when clinical findings were also taken into account. (7 Refs) (In CHI)

2. HETEROGENEOUS PITUITARY ADENOMAS. A LIGHT MICROSCOPIC, IMMUNOHISTOCHEMICAL AND ELECTRON MICROSCOPIC STUDY.

Martinez D, Barthe D
Laboratoire d'Histologie, Faculte de Medecine, 2 rue du Docteur Marcland, F-87032 Limoges, Cedex, France
Virchows Arch [Pathol Anat]; 394(3):221-233 1982

The combined use of several histological procedures (ie conventional light microscopy, immunohistochemistry and electron microscopy) among 45 unselected pituitary adenomas demonstrated the existence of nine tumors (20%) containing several identifiable adenohypophyseal cell types. The cellular associations were between two or three identifiable cell types. Mammosomatotrophic tumors were the most frequent but not the only mixed type (somatomammocorticotrophic, somatocorticotrophic tumors were also found). The cellular components varied in size, but the cells appeared randomly distributed in the tumors. In all the adenomas there was an unidentified cell component (no reactivity with antisera used) varying from sparse to numerous elements. On adjacent sections the adenomatous cells reacted with a single specific antiserum, but in two cases the immunohistochemistry on contiguous paraffin embedded sections did not confirm this with certainty. These results confirm those of others and a new term is purposed to designate these tumors: heterogeneous pituitary adenomas. According to the nature and the proportions of the cell components, the heterogeneous adenomas were subdivided into two groups: a group A which comprised adenomas formed by a major identifiable cellular type associated with one or two other less frequent cell types, and a group B formed by a predominant unidentifiable (no reactivity with immunochemical stainings) cell type associated with one or two other identified cell types. The present morphofunctional classifications of pituitary adenomas should be modified to include homogeneous adenomas with a single cell type and heterogeneous adenomas with several cell types. (Author abstract) (39 Refs)

3. PITUITARY ADENOMAS WITH HYPERFUNCTION OF TSH. FREQUENCY, HISTOLOGICAL CLASSIFICATION, IMMUNOCYTOCHEMISTRY AND ULTRASTRUCTURE.

Saeger W, Ludecke DK
Abteilung fur Pathologie, Marienkrankenhauses Hamburg, Alfredstrasse 9, D-2000 H amburg 76, W. Germany
Virchows Arch [Pathol Anat]; 394(3):255-267 1982

In a collection of 564 surgically removed pituitary adenomas, four cases were found to have had elevated TSH plasma levels. One of these tumors (case 1) could be classified as a highly differentiated mucoid TSH cell adenoma presenting histochemical reactions typical of, as well as electron microscopical features identical to, normal TSH cells. Immunoenzymatic studies failed to demonstrate TSH in the tumor cells. Two further adenomas (case 2 and 3) were similarly structured in many areas, but showed regions of poorer differentiation in which cells with distinct pleomorphism, irregular secretory granules, increased numbers of ribosomes and a well developed rough endoplasmic reticulum were present. In 10% of the tumor cells GH could be demonstrated immunoenzymatically, but there was no TSH. The fourth adenoma was an undifferentiated acidophilic adenoma showing pleomorphic cells having slight acidophil and partly mucoid granulations. The ultrastructure showed convoluted nuclei, increased numbers of free ribosomes as well as abundant rough endoplasmic reticulum and secretory granules which were different in size and number but distinctly of the TSH cell type. Immunoenzymatically, TSH was found in some cells, with GH in more cells. Endocrinologically, elevated levels of GH were measured in cases 2, 3 and 4 with LH being increased in case 1. Clinical and morphological correlations are discussed. (Author abstract) (39 Refs)

4. SURGICAL TREATMENT OF PITUITARY ADENOMAS. AN ANALYSIS OF 188 CASES.

Haguenauer JP, Goutelle A
Service d'O.R.L., Hopital de la Croix-Rousse, F 69317 Lyon, France
Ann Otolaryngol Chir Cervicofac; 98(4/5):207-212 1981

In a series of 204 operations for pituitary tumors, 16 were performed for local recurrence. Visual symptoms were the most common and were found in 119 patients (63.3%). Headaches affected 50 patients. Hypersecreting adenomas were diagnosed in 97 cases (58 growth hormone adenomas, 36 prolactin adenomas, 2 corticotropic adenomas, and 1 gonadotropic adenoma). Hypofunctional adenomas were discovered in 83 patients, and oncocytomas were diagnosed in five patients. A Water's view plain film and tomographic scan revealing destruction or changes in the sella turcica are generally sufficient to make the diagnosis. In 27 cases, the intracranial approach was used in surgery, and in 173 cases, the naso-sphenoidal approach was used. Presurgical radiotherapy was used in 18 patients, and complementary radiotherapy was delivered in 50% of the cases. The visual symptomatology improved in 40 cases, but in 10 cases, there was early postoperative aggravation of the visual problems and in six cases, delayed aggravation following a remission phase. The most dependable criteria for suspecting local tumor recurrence was secondary mod ification of the visual field which occurred in all 16 cases in this series. (no Refs) (In FRE)

5. SUBSTANTIATION OF THE SURGICAL MANAGEMENT OF RECURRENT PITUITARY ADENOMAS.

Patsko IaV
Res. Inst. Neurosurgery, Kiev, USSR
Klin Khir; (12):22-26 1981

Of 339 patients subjected to surgery for pituitary adenomas, 37 (18 men, 19 women; 22-50 yr old) had recurrent tumors. Histologically, 21 patients had chromophobe adenomas, 9 had mixed tumors, and 7 had eosinophilic adenomas. Of 37 patients, 26 developed recurrences within the first 5 yr after the surgery. Recurrent adenomas were characterized by extrasellar dissemination and infiltration of the cavernous sinuses. Early clinical manifestations of recurrent pituitary adenomas included cerebral symptoms, headache, and oculomotor disorders. Progressive pituitary hyperfunction was observed only in the patients with hormone-active adenomas. It was recommended that the patients with continuous growth of pituitary adenomas should undergo subtotal or partial removal of the tumor. Radical surgery is associated with the risk of an injury of mediobasal regions of the brain. (4 Refs) (In RUS)

6. DENTAL CONSIDERATIONS IN THE SUBLABIAL TRANS-SPHENOIDAL SURGICAL APPROACH TO THE PITUITARY GLAND.

Watson SW, Sinn DP, Neuwalt EA, Laws ER, Angelillo JC
(c/o Neuwelt) Dept. Surgery, Div. Neurosurgery, Univ. Oregon Health Science Center, 3181 Southwest San Jackson Park Road, Portland, OR, 97201
Neurosurgery; 10(2):236-241 1982

Pulpal injury and devitalization of anterior teeth can be avoided in the sublabial trans-sphenoidal surgical approach to the pituitary gland by preoperative evaluation of skeletal and dental morphology. The amount of bone between the tooth roots and nasal floor determines whether the nasal retractor will have sufficient room. Facial morphology is discussed with respect to vertical maxillary deficiency and excess. The former skeletal form leaves little space for placement of the nasal retractor without injury to the maxillary incisors. (10 Refs)

7. TREATMENT OF ACROMEGALY BY TRANS-SPHENOIDAL OPERATION, 90-YTTRIUM IMPLANTATION AND BROMOCRIPTINE: RESULTS IN 230 PATIENTS.

Quabbe HJ, Buch K, Solbach HG, Wiegelmann W, Benker G, WindeckR, Allhoff PH, Kobberling J, Mayer G, Ludecke DK, SchraderD, Lucke C, Wagner TO, Winkelmann W, Heesen D, Wilcke O, von Werder K, Fahlbusch R
Klinikum Steglitz, Hindenburgdamm 30, D-1000 Berlin 45, W. Germany
Clin Endocrinol (Oxf); 16(2):107-119 1982

Two hundred and thirty patients with acromegaly were diagnosed and treated in a prospective cooperative study in 12 university clinics. Primary treatment was: trans-sphenoidal surgery (152 patients), trans-sphenoidal surgery with additional cryotherapy (18 patients), Yttrium-90-implantation (30 patients), bromocriptine (30 patients). The results of endocrine assessment before treatment and 6 mo after operation, 90-Y implantation or commencement of bromocriptine therapy are reported. The best results (low GH, no or little deterioration of pituitary function, low complication rate) were achieved by trans-sphenoidal surgery, especially in patients with intrasellar tumors (basal GH less than 5 ng/ml in 59.7%). Results were less good with increasing tumor size. Additional cryosurgery was accompanied by a high rate of anterior pituitary insufficiency and is no longer employed. Yttrium-90-implantation resulted in less improvement in GH levels (basal GH less than 5 ng/ml in 51.7% of patients with intrasellar tumors), a high rate of pituitary insufficiency and more complications. Bromocriptine treatment was least effective in lowering GH concentrations (basal GH less than 5 ng/ml in 33% of patients with intrasellar tumors). Different criteria for treatment success were compared. In the entire group, basal GH concentrations below 5 ng/ml were attained in 51.7% of all patients whose values were higher than this prior to treatment. Suppressibility of GH below 2 ng/ml during glucose loading occurred in only 34.9%. An abnormal GH response to TRH/LHRH was present in 47.2% before and in 43.4% after/during treatment. The prognostic significance of this latter finding must be evaluated by further study. (Author abstract) (32 Refs)

8. THE RECOVERY OF THE HYPOTHALAMO-PITUITARY-ADRENAL AXIS AFTER TRANSSPHENOIDAL OPERATION IN THREE PATIENTS WITH CUSHING'S DISEASE. THE EFFECT OF PRIOR EXTERNAL PITUITARY IRRADIATION.

Lamberts SW, Klijn JG, De Jong FH, Birkenhager JC
Dept. Medicine, Univ. Hosp. Dijkzigt, 40 Dr. Molewaterplein, 3015 GD Rotterdam, The Netherlands
Acta Endocrinol (Copenh); 98(4):580-585 1981

The recovery of the hypothalamo-pituitary-adrenal axis after selective transsphenoidal adenomectomy was studied in three patients with Cushing's disease by measuring basal plasma ACTH and cortisol concentrations, cortisol secretion rate, the diurnal rhythm of cortisol, and the reaction of cortisol to lysine vasopressin (LVP), of compound S to metyrapone and of cortisol and growth hormone to an insulin-induced hypoglycemia. The third patient had been treated previously by external pituitary irradiation. In two patients basal plasma ACTH levels returned within normal values before plasma cortisol, but no supra-physiological plasma concentrations of ACTH were seen as has been observed after withdrawal of exogenous glucocorticoids. With regard to the different stimulation tests: at first the normal reaction of plasma cortisol to LVP returned after 3 mo, at the same time as the restoration of growth hormone secretion in response to hypoglycemia. A normalization of the reaction to metyrapone was seen thereafter while finally the reaction of cortisol to an insulin-induced hypoglycemia and the diurnal rhythm of plasma cortisol returned 15 to 18 mo after operation in the first patient and after 12 mo in the second patient. Selective adenomectomy had also been carried out in the third patient, as evidenced by normal TSH, LH, and FSH secretion. Hypocortisolism, and a deficient ACTH and growth hormone secretion in response to the stimuli mentioned, however, did not normalize up till 22 mo after operation. The restoration of the hypothalamo-pituitary-adrenal axis after selective pituitary adenomectomy in Cushing's disease was prevented in this patient by prior external pituitary irradiation. (Author abstract) (11 Refs)

9. SIZE REDUCTION OF EXTRASELLAR PITUITARY TUMORS DURING BROMOCRIPTINE TREATMENT: QUANTITATION OF EFFECT ON DIFFERENT TYPES OF TUMORS.

Wollesen F, Andersen T, Karle A
Div. Endocrinology, Hvidovre Hosp., 2650 Hvidovre, Denmark
Ann Intern Med; 96(3):281-286 1982

The well-known size-reducing effect of bromocriptine on prolactinomas was tested on five types of large, extrasellar pituitary tumors. Twenty patients were treated prospectively for up to 4.5 years with bromocriptine, 30 or 60 mg/day (2 patients received 15 mg and 160 mg, respectively). The effect on the size of the pituitary tumors was quantitated by planimetry of computed tomographic scans before and during treatment. The immediate success rate was 16 of 20 tumors. Eleven nonsecreting tumors were reduced by a median of 32% (range of reduction for 50% of cases, 18%-41%) with an immediate success rate of 9 of 11. Nine secreting tumors (4 that secreted prolactin; 3, growth hormone; 1, adrenocorticotropic hormone; and 1, thyroid stimulating hormone) were reduced by a median of 51% (range of reduction for 50% of cases, 25%-72%). The reduction in tumor size was significantly associated with pretreatment size (r = 0.6360, p less than 0.005), but not with the serum concentration of any hormones assayed or previous radiation treatment. Bromocriptine causes a clinically significant reduction in size of nonsecreting as well as secreting pituitary tumors with the same success rate as that of conventional treatments. (Author abstract) (35 Refs)

10. HYPERPROLACTINAEMIA IN MEN - RESPONSE TO BROMOCRIPTINE THERAPY.

Prescott RW, Kendall-Taylor P, Hall K, Johnston DG, Crombie A, McGregor A, Hall R
Dept. Medicine, Univ. Newcastle upon Tyne, Newcastle upon Tyne NE1 4LP, England
Lancet; 1(8266):245-249 1982

Men with hyperprolactinemia present with large tumors. Conventional therapy with surgery and/or irradiation is unsatisfactory, with up to 100% of patients remaining hyperprolactinemic (or subsequently developing pituitary insufficiency). In view of reports of bromocriptine-induced regression of prolactinomas, eight consecutive male hyperprolactinemic patients with impotence and/or symptoms rela ted to local tumor effects were treated with bromocriptine 20 mg daily as sole therapy for 3-11 mo. Symptoms were relieved partly or completely in seven patients and serum prolactin was restored to normal or near normal in all men. Serum thyroxine and plasma cortisol response to hypoglycemia became normal in two men who had subnormal values before therapy. Mean serum growth hormone response to hypoglycemia rose significantly as did plasma testosterone concentrations. Evidence of tumor regression, sometimes massive, was seen in the six patients who underwent repeat radiology. The symptomatic relief and biochemical and radiological improvement in these patients indicate that bromocriptine therapy may now be the treatment of choice for hyperprolactinemic men with large tumors. (Author abstract) (37 Refs)

11. DILEMMAS IN THE MANAGEMENT OF FUNCTIONING PITUITARY TUMOURS.

McGregor AM, Gisberg J
Welsh Natl. Sch. Medicine, Cardiff, Wales
J Appl Med; 8(2):117,119,121,123 1982

Controversy over the management of pituitary tumors, particularly prolactin-secreting adenomas, is discussed. Radiological assessment, endocrine assessment and treatment modalities are described. The mode of therapy is too often based on the expertise and equipment available with little effort made to compare the various therapeutic regimens. Conventional external irradiation to the pituitary has a delayed effect in controlling the growth of the tumor and may produce unacceptable and unpredictable side effects. In patients with acromegaly, radiotherapy produces disease control as well as other modes of therapy after long-term follow-up. Small adenomas secreting prolactin are best treated by the trans-sphenoidal surgical approach. Bromocriptine (BRO) is useful for treating prolactinomas of any size. Trans-sphenoidal removal of adenomas secreting growth hormone is recommended. Adenomas of corticotrophic cells are best treated with bilateral adrenalectomy with steroids. Drug therapy may be useful for these tumors, but relapse occurs when the drugs are withdrawn. Pituitary microsurgery is advocated for treatment of adults with small corticotrophic cell adenomas. Long-term follow-up data on patients with pituitary tumors is limited and success of therapy, recurrence rates, and side effects need to be evaluated. (50 Refs)

12. PRECOCIOUS PUBERTY ASSOCIATED WITH CRANIOPHARYNGIOMA. A CASE REPORT.

Forman MB, Kalk WJ, Griffiths J
(c/o Kalk) Dept. Medicine, Medical Sch., Esselen St., Hillbrow, Johannesburg, 2001, South Africa
S Afr Med J; 61(7):245-247 1982

Craniopharyngiomas in children are usually associated with growth retardation and hypogonadism. A patient with a craniopharyngioma treated with radiotherapy, who later developed isosexual precocious puberty, is described. She was treated with cyproterone acetate with a good clinical respons e. We suggest that craniopharyngiomas may become a more frequent cause of precocious puberty now that conservative therapy has been advocated for the condition. (Author abstract) (11 Refs)

13. PINEAL REGION MENINGIOMAS WITHOUT DURAL ATTACHMENT.

Roda JM, Perez-Higueras A, Oliver B, Alvarez MP, Blazquez MG
Caleruega 22, Madrid 33, Spain
Surg Neurol; 17(2):147-151 1982

A rare case of meningioma in the pineal region without dural attachment, which was successfully removed through an infratentorial supracerebellar approach, is presented. The preoperative diagnosis was made by means of computed tomography together with histographic analysis. We review similar cases reported in the literature and discuss the clinical features, diagnostic aspects, and surgical management. (Author abstract) (24 Refs)

THYROID TUMORS

14. COMPARISON OF TI-201 CHLORIDE AND GA-67 CITRATE SCINTIGRAPHY IN THE DIAGNOSIS OF THYROID TUMOR: CONCISE COMMUNICATION.

Senga O, Miyakawa M, Shirota H, Makiuchi M, Yano K, Miyazawa M, Takizawa M
Dept. Surgery, Faculty Medicine, Shinshu Univ., 3-1-1, Asahi, Matsumoto, Nagano 390, Japan
J Nucl Med; 23(3):225-228 1982

Twenty-five patients with thyroid tumors were scintigraphed with both TI-201 chloride and Ga-67 citrate. All cases showed a focal area of decreased activity with I-131 or pertechnetate (Tc-99m), and each had a histological diagnosis after surgery or excisional biopsy. From the data we conclude the following: (1) Tumors giving a positive scan with TI-201 chloride but negative results using Ga-67 citrate prove to be differentiated carcinoma or poorly differentiated adenoma. (2) All tumors that are positive with Ga-67 are highly malignant types, and if these tumors are negative by Tl-201, undifferentiated carcinoma is suggested. (3) Ga-67 citrate scintigraphy is a useful procedure in locating distant metastases, in determining the area to be irradiated, and in judging the effect of therapy on undifferentiated carcinoma. (Author abstract) (13 Refs)

15. CRITICAL EVALUATION OF SERUM THYROGLOBULIN LEVELS AND I-131 SCANS IN POST-THERAPY PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA: CONCISE COMMUNICATION.

Echenique RL, Kasi L, Haynie TP, Glenn HJ, Samaan NA, Hill CS
P.O. Box 36734, Houston, TX, 77036
J Nucl Med; 23(3):235-240 1982

Serum thyroglobulin measurements by radioimmunoassay were performed in the follow-up of 68 patients with differentiated thyroid carcinoma undergoing I-131 total-body scans following surgery and/or I-131 therapy. Of 12 patients with distant metastases demonstrated by I-131 scan, thyroglobulin levels were elevated (greater than 60 ng/ml) in 9 (75%); the remaining 25% either ranged between 20 and 60 ng/ml or were below 20 ng/ml in spite of having functional metastases. Of six patients with only regional lymph- node metastases demonstrated by I-131 scan, only one (16%) had an elevated thyroglobulin level, while two fell in the 20-60 ng/ml range and three were below 20 ng/ml. Of the remaining patients with no metastatic disease demonstrable by I-131 scan, three (6%) had elevated thyroglobulin levels. These patients were subsequently found to have metastatic disease by other criteria. These results suggest caution in the use of thyroglobulin levels as a replacement for I-131 scans in the follow-up of differentiated thyroid carcinoma. Based on our study, however, the two methods complement each other to achieve maximum sensitivity and reliability. (Author abstract) (12 Refs)

16. CT DIAGNOSIS OF MEDIASTINAL THYROID.

Glazer GM, Axel L, Moss AA
Dept. Radiology, Univ. Michigan Medical Center, Ann Arbor, MI, 48109
AJR; 138(3):495-498 1982

Computed tomography (CT) is capable of specifically diagnosing mediastinal thyroid as the cause of a mediastinal mass. Five representative cases illustrate characteristic features of substernal thyroid. These include: (1) anatomic continuity with the cervical thyroid; (2) focal calcifications; (3) relatively high CT number; (4) rise in CT number after bolus administration of iodinated urographic contrast material; and (5) prolonged enhancement after contrast administration. While not all of these features are present in each case, a combination of these should permit accurate diagnosis in most cases. (Author abstract) (10 Refs)

17. INDIRECT THYROID LYMPHOGRAPHY IN DIAGNOSIS OF THYROID DISEASES.

Kradinov AI, Fesenko VP, Kabalich AK
Dept. Roentgenology and Radiology, Crimean Medical Inst., Simferopol, USSR
Vestn Rentgenol Radiol; (6):63-67 1981

Diagnostic efficacy of indirect thyroid lymphography was evaluated in 232 patients (31 men, 201 women; 9-80 yr old) with various thyroid diseases. Among these patients, 59 had diffuse goiter, 89 had nodular goiter, 48 had mixed goiter, 20 had recurrent goiter, 6 had Hashimoto thyroiditis, and 10 had thyroid cancer. The intrastitial administration of the contrast medium provided reliable information on the size of the thyroid, the state of microcirculation, and the type of the lesion. The lymphographic data coincided with the intraoperative findings in 91.9% of the patients. (13 Refs) (In RUS)

18. THE ULTRASTRUCTURE OF THE THYROID MEDULLARY CARCINOMA.

Tasca C, Stefaneanu L
Inst. Endocrinology, Bucharest, Romania
Morphol Embryol (Bucur); 27(4):335-340 1981

Ultrastructure and secretory granules were studied in six cases of thyroid medullary carcinoma. Tumor cells were either fusiform or showed a polyhedral appearance. Dilated, rounded, or ovoid sacks and small vesicles were observed in the rough endoplasmic reticulum. Numerous round-shaped electron-dense secretory granules various in size were also present. Results indicate either the dependency of granules size on the maturation degree and the functional activity, or the existence of several kinds of granules specialized in the secretion of various substances. (24 Refs)

19. SURGICAL TREATMENT OF MEDULLARY THYROID CARCINOMA.

Roka R, Niederle B, Fritsch A, Krisch K, Schemper M
I. Chirurgische Universitatsklinik, Spitalgasse 2, A-1090 Wien, Austria
Dtsch Med Wochenschr; 107(4):132-138 1982

The postoperative course of sporadic medullary thyroid carcinoma was correlated retrospectively in 19 patients with the primary surgical treatment. Besides prognostic factors such as lymph node involvement (clinically in 21%, microscopically in 42%, among these 29% in the upper anterior mediastinum) and distant metastases (11%), differences were seen between the group with negative lymph node involvement and primarily nonradical treatment (Group 1) and with primarily radical surgery and equal tumor stage (Group 2): In Group 1 local recurrences were observed in four out of six patients as a sign of remaining tumor tissue. In addition three out of six patients showed lymph nodes, two had multiple distant metastases at the time of the second surgical intervention. In two patients increased basal and stimulated calcitonin levels indicted clinically occult distant metastases. Two patients died of medullary thyroid carcinoma, another has a cervical recurrence. No patient of Group 2 had to be reoperated within the observation period (6-101 mo) or has died of medullary thyroid carcinoma. Lymph node involvement was investigated in nine patients with modified radical cervical dissection (nerves and sternocleidomastoid muscle remained untouched). Metastases involving upper and lower jugular lymph node groups were found as a rule and further involvement of lymph nodes in the upper anterior mediastinum. Primary surgical intervention in sporadic medullary thyroid carcinoma should comprise total thyroidectomy with diagnostic lymphadenectomy. According to the results a modified radical neck dissection with dissection of the upper mediastinum, ie, as radical a surgical technique as possible, should be mandatory. (Author abstract) (38 Refs) (In GER)

20. MULTIPLE ENDOCRINE NEOPLASIA TYPE 2B IN TWINS.

Galera H, Gonzales-Campora R, Matilla A, Martin I
Hosp. Universitario de la Facultad de Medicina, Avda. Dr. Fedriani S/N, Sevilla, Spain
Histopathology; 6(1):111-119 1982

Medullary carcinomas of the thyroid associated with Marfan-like features and multiple neuromas were observed in female twins (14 yr old). Dark coloration of skin, scanty genital development, thick and prominent lips, and numerous small nodular masses in the tongue were observed in both patients. Following diagnosis of multiple endocrine neoplasia (MEN) type 2b without clinical involvement of the a drenal medulla, total thyroidectomy with dissection of cervical lymph nodes was performed in both patients. Postoperatively, serum calcitonin levels returned to normal in one patient but remained elevated in the other. The second patient has been treated with adriamycin. (20 Refs)

21. THYROID MALIGNANCY IN THE ELDERLY.

Simpson WJ
Dept. Radiation Oncology, Princess Margaret Hosp., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada
Geriatrics; 37(3):119-121,124-125 1982

Pathogenesis, diagnosis, therapy, follow-up care, complications, and prognosis of thyroid malignancy (TM) in the elderly are described. Patients with follicular and anaplastic tumors (approx 50%) and with papillary cancers (approx 33%) gave a history of a goiter that had been unchanged for many yr but had grown recently. The most common clinical manifestation is a mass in the lower neck or enlargement of a preexisting goiter. Radioiodine scanning, ultrasonography, and fine needle aspiration are performed. Patients with clinically evident cancers require a search for metastases, using chest x-ray, bone scan, or skeletal x-rays, liver function tests, and liver and brain scan. Surgery is indicated in almost all patients. Radioiodine is important in treatment of papillary and follicular thyroid cancers. External radiation may play a vital role for every type of TM. Thyroid hormone should be administered to inhibit thyroid-stimulating hormone release and to provide replacement therapy where the disease or the treatment left insufficient thyroid tissue to maintain the euthyroid state. Complications include spinal cord compression caused by an extradural tumor originating in a vertebral body and surgical complications that may occur with any thyroid operation. Pulmonary fibrosis and spinal cord necrosis are serious complications caused by external radiation. The prognosis for elderly patients with TM is much graver than for younger ones, and the treatment must be more aggressive, emphasizing the need for early diagnosis with prompt investigation and treatment. (9 Refs)

22. MORTALITY IN WOMEN TREATED BY HYPERTHYROIDISM.

Hoffman DA, McConahey WM, Diamond EI, Kurland LT
Environmental Epidemiology Branch, NCI, Rm. 3C-07, Landow Bldg., Bethesda, MD, 20205
Am J Epidemiol; 115(2):243-254 1982

To evaluate the late effects of exposure to radioiodine (131I), a retrospective cohort study was conducted of women treated for hyperthyroidism at the Mayo Clinic, Rochester, Minnesota, from 1946 through 1964. Cause of death was determined in 1,005 women treated with 131I and in 2,141 women surgically treated. No increased risk of total mortality was observed for the 131I-treated women (relative risk = 1.0). There were no increased risks for the major causes of mortality (cancer, cardiovascular-renal disease or cerebrovascular lesions) in the 131I-treated women; in addition, there were no increased risks for site-specific cancer mortality. Several hypotheses are presented to suggest reasons for the lack of association between 131I exposure and increased cancer mortality. (Author abstract) (41 Refs)

23. PRIOR IRRADIATION AND THE DEVELOPMENT OF COEXISTENT DIFFERENTIATED THYROID CANCER AND HYPERPARATHYROIDISM.

Prinz RA, Barbato AL, Braithwaite SS, Brooks MH, Lawrence AM, Paloyan E
Dept. Surgery, Loyola Univ., Stritch Sch. Medicine, 2160 South First Ave., Maywood, IL, 60153
Cancer; 49(5):874-877 1982

Twelve patients with coexistent well-differentiated thyroid carcinoma and primary hyperparathyroidism were studied to determine the frequency of previous radiation exposure. Eight were found to have received prior irradiation. External radiation was administered to the head and neck region for benign conditions such as tonsillar enlargement, acne, scrofula, and thyroid enlargement. One patient received 131I therapy for carcinoma of the thyroid. The observation that 67% of the patients in this series had previous radiation to the head and neck strongly implicates radiation exposure in the development of coexistent well-differentiated thyroid carcinoma and hyperparathyroidism. (Author abstract) (28 Refs)

24. THYROID HYPOFUNCTION AFTER EXPOSURE TO FALLOUT FROM A HYDROGEN BOMB EXPLOSION.

Larsen PR, Conard RA, Knudsen KD, Robbins J, Wolff J, Rall JE, Nicoloff JT, Dobyns BM
Dept. Medicine, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
JAMA; 247(11):1571-1575 1982

Thyroid function was evaluated in the Marshallese who were accidentally exposed to fallout-containing radioiodine isotopes in 1954. Measurements of thyrotrophin (TSH, thyroid-stimulating hormone) levels and free thyroxine (T4) index (FT4I) have revealed that, among 86 persons exposed on Rongelap and Allingnae atolls, 14 have shown evidence of thyroid hypofunction. This was first noted in some individuals about 10 years after exposure. Only two of these showed clinical evidence of hypothyroidism. The most marked TSH elevations were noted in nine persons exposed when younger than 6 years, with estimated doses to the thyroid from 390 to 2,100 rad. Most of this group subsequently had surgery for removal of thyroid nodules. The remaining five cases have been noted more recently among 36 surviving adults exposed at an older age who showed no other detectable thyroid abnormalities. This group had received estimated thyroid doses ranging from 135 to 335 rad and showed modest elevation of serum TSH levels (6 to 9 uU/mL) and a slightly subnormal FT4I. No abnormalities were found in persons on Utirik who received substantially less radiation, and hypothyroidism was present in less than 1% of the control, unexposed Marshallese. The high prevalence of a thyroid hypofunction in these persons indicates that this condition, as well as thyroid nodularity, can be a delayed complication of exposure to early fallout from a nuclear explosion. The fact that a significant fraction of the radiation to the thyroid was from short-lived radioiodine isotopes (132I, 133I, 136I), as opposed to 131I, may account for the severity of the thyroid damage. (Author abstract) (20 Refs)

PARATHYROID TUMORS

25. RADIOGRAPHIC FINDINGS IN RECURRENT PARATHYROID CARCINOMA.

Krudy AG, Doppman JL, Marx SJ, Brennan MF, Spiegel A, Aurback GD

(c/o Doppman), NIH, Room 6S211, Building 10, Bethesda, MD, 20205

Radiology; 142(3):625-629 1982

Seven cases of recurrent parathyroid carcinoma were reviewed. Subperiosteal resorption was seen in six, pulmonary nodules in four, renal calculi in five, brown tumors in five, and pancreatic calcifications in one. Angiography was performed in five patients, showing one definite and two probable cervical recurrences, one mediastinal lesion, and one case of possible bone metastases. Venous sampling for parathyroid hormone was carried out in four patients and suggested residual disease in two; in addition, there were one false and one true negative. CT was performed in four patients and was useful in delineating metastatic pulmonary nodules, cervical recurrence, and hepatic metastases. The radiographic approach to recurrent parathyroid carcinoma and the use of CT and angiography are discussed. (Author abstract) (10 Refs)

26. ABNORMAL BONE AND PARATHYROID HISTOLOGY IN CARCINOMA PATIENTS WITH PSEUDOHYPERPARATHYROIDISM.

Sharp CF, Rude RK, Terry R, Singer FR

Dept. Medicine, LAC/Univ. Southern California Medical Center, Room 6442, 1200 North State St., Los Angeles, CA, 90033

Cancer; 49(7):1449-1455 1982

Postmortem bone and parathyroid gland histology in nine hypercalcemic cancer patients without bone metastases was compared to bone and parathyroid histology in 10 normocalcemic patients. Parameters of parathyroid function, including serum immunoreactive parathyroid hormone, acid base status, serum phosphate, and nephrogenous cyclic AMP were measured in the hypercalcemic group and compared to normals and to patients with primary hyperparathyroidism. Bone histology in all nine hypercalcemic cancer patients showed increased osteoclastic bone resorption and increased fibrous connective tissue in the bone marrow. Parathyroid glands were of normal size in all nine patients but contained little or no fat, one criterion of parathyroid hyperplasia. In the normocalcemic cancer patients only 2/10 had minimally increased bone resorption while 7/10 had decreased or absent stromal fat in the parathyroid glands. Despite the hyperplastic appearance of the parathyroid glands, serum biochemical parameters in the hypercalcemic cancer patients indicate a state of suppressed parathyroid function suggesting that the osteoclastic bone resorption is related to a humoral substance elaborated by the tumors which is distinct from parathyroid hormone. (Author abstract) (30 Refs)

ADRENAL TUMORS

27. LIMITATIONS, POSSIBILITIES, AND PROSPECTS OF X-RAY EXAMINATION IN DIAGNOSIS OF ADRENAL DISEASES.

Bukhman AI

Inst. Experimental Endocrinology and Chemistry of Hormones, Moscow, USSR

Probl Endokrinol (Mosk); 28(1):51-56 1982

Diagnostic efficacy of x-ray examination was studied in 250 patients (18-63 yr old) with various pathological changes of the adrenal glands. Group 1 consisted of 125 patients who underwent single pneumography, and Group 2 consisted of 125 patients subjected to repeated pneumography. The x-ray diagnosis was compared with operative findings. In Group 1, correct preoperative diagnosis was made in 119/125 patients (25/27 with tumors of the adrenal cortex, 26/26 with tumors of the adrenal medulla, and 68/72 with Cushing's disease). Pneumography did not show 0.7 x 0.5-cm aldosteroma of the right adrenal and 4 x 4-cm corticosteroma of the right adrenal. Repeated pneumography was less effective: correct preoperative diagnosis was made only in 99/125 patients from Group 2. The patients who underwent unsuccessful pneumography were subjected to selective venography or infusion urography. (12 Refs) (In RUS)

28. VALUE OF COMPUTED TOMOGRAPHY OF THE ABDOMEN AND CHEST IN INVESTIGATION OF CUSHING'S SYNDROME.

White FE, White MC, Drury PL, Fry IK, Besser GM

Dept. Radiology, St. Bartholomew's Hosp., London EC1A 7BE, England

Br Med J; 284(6318):771-774 1982

Computed tomography (CT) scans were performed on 37 patients with biochemically proven Cushing's syndrome to evaluate the role of CT in the investigation of this condition. CT rapidly and correctly identified all 15 adrenocortical tumors, distinguishing 5 carcinomas from the 10 adenomas. In ACTH-dependent Cushing's syndrome appreciable bilateral adrenal enlargement was common in patients with an ectopic source (6 of 10 cases), while those with a pituitary source usually had normal sized adrenals (9 of 10). Two patients with a history of over 7 yr had bilateral adrenal nodules. CT was more accurate in locating a primary ectopic source of ACTH (5 of 12 cases) than any other technique and was particularly valuable in detecting small (less than 1.5 cm) peripheral lung carcinoid tumors which may be undetectable by conventional x-ray techniques. Its speed, accuracy, and simplicity make CT the technique of choice both to show the adrenal anatomy and to locate a suspected ectopic ACTH-secreting tumor in patients with proven Cushing's syndrome. (Author abstract) (18 Refs)

29. RADIOLOGY OF PHEOCHROMOCYTOMAS.

Amorosa LF, Amorosa JK, Nosher JL, Donnelly B

Dept. Medicine, Rutgers Medical Sch., UMD, P.O. Box 101, Piscataway, NJ, 08854

J Med Soc NJ; 79(2):114-117 1982

The site of a pheochromocytoma can be assessed fairly accurately by considering the patient's age, family history, and evidence of other endocrine tumors or neurocutaneous diseases. In 90% of cases, the tumor is sporadic (nonfamilial). Such patients are usually 40-60 yr old; about 85% of the tumors are confined to one adrenal and the remaining 15% are bilateral or extra-adrenal. Familial cases are associated with two entities transmitted by an autosomal dominant gene. In the multiple endocrine neoplasia Type II (MEN-II) syndrome, pheochromocytoma is associated with medullary carcinoma of the thyroid, parathyroid hyperplasia, and occasionally oral and cutaneous neuromas. Symptoms of pheochromocytoma usually develop in patients 25-40 yr old; the tumors are almost always intra-adrenal and bilateral. In simple familial pheochromocytoma, sustained hypertension is diagnosed in youth (av 20 yr old); the tumors are commonly bilateral and extra-adrenal and may recur after surgery. Similar characteristics may be found in children and adolescents with sporadic pheochromocytomas. Patients with familial neuroectodermal diseases (von Recklinghausen or von Hippel-Lindau syndrome) may also develop pheochromocytomas, some of which are bilateral. Extra-adrenal (ectopic) pheochromocytomas or paragangliomas usually arise adjacent to sympathetic ganglia. Only 1% of these tumors arise in supradiaphragmatic sites. Malignant changes (demonstrable metastases, locally or in the lungs or liver) develop in 25% of pheochromocytomas associated with the MEN-II syndrome and in 10-15% of sporadic pheochromocytomas in adults. The frequency may be higher in familial tumors. Malignancy is rare in children or adolescents. Pheochromocytomas can be localized by iv urography and angiography, but the studies carry a risk of hypertensive paroxysm induced by the contrast medium. Computed tomographic and ultrasound scans can accurately localize a pheochromocytoma without risk to the patient. (22 Refs)

30. CUSHING'S SYNDROME IN PREGNANCY - TREATMENT WITH METYRAPONE.

Gormley MJ, Hadden DR, Kennedy TL, Montgomery DA, Murnaghan GA, Sheridan B

(c/o Hadden) Metabolic Unit, Royal Victoria Hosp., Belfast BT12 6BA, Ireland

Clin Endocrinol (Oxf); 16(3):283-293 1982

A 23-yr-old female presented with severe Cushing's syndrome in the 23rd wk of pregnancy. Investigations showed plasma cortisol 770 nmol/l (08.00 hr) and 850 nmol/l (23.00 hr); plasma ACTH was 10 ng/l (08.00 hr) and 27 ng/l (23.00 hr); urinary free cortisol excretion was 2,460 nmol/24 hr. Dexamethasone 2 mg 6-hourly for 48 hr suppressed the 08.00 hr plasma cortisol only to 680 nmol/l. Abdominal CT scan showed a right adrenal adenoma. The patient was treated with metyrapone and a good clinical improvement ensued. Plasma cortisol was reduced to 300-500 nmol/l. Despite ultrasonographic evidence of normal fetal growth, urinary estriol excretion was markedly deficient. Prior to the spontaneous onset of labor, there was a marked rise in plasma cortisol despite continuous metyrapone treatment. A normal female infant was born at 37 wk gestation. The maternal adrenal adenoma was subsequently removed. The deficiency of estriol synthesis during the pregnancy may be explained by metyrapone-induced inhibition of C19-hydroxylation. (Author abstract) (42 Refs)

PANCREAS TUMORS

31. RAPID RADIOIMMUNOASSAY FOR INSULIN AND ITS APPLICATION IN LOCALIZING OCCULT INSULINOMAS BY INTRAOPERATIVE PANCREATIC VEIN CATHETERIZATION.

Zick R, Hammer A, Otten G, Mitzkat HJ

Zentrum Innere Medizin und Dermatologie, Arbeitsbereich, Diabetologie Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, W. Germany

Eur J Nucl Med; 7(2):85-87 1982

Intraoperative pancreatic vein catheterization at laparotomy and immediate insulin determination of serum samples by rapid radioimmunoassay (RIA) allows localization of insulinomas during surgery and avoids risk of transhepatic catheterization. Two cases are described in which sonography, computed tomography, and selective arteriography did not yield clear diagnosis, but RIA of serum collected intraoperatively helped locate tumors. Serial sampling of tributaries to the vena mesenterica superior and vena lienalis showed locations of elevated insulin levels, which were confirmed by immediate resection of benign insulinomas in both cases. Removal of tumors were followed rapidly by reduced serum insulin levels. (10 Refs)

32. GLUCAGONOMA SYNDROME IN A CASE OF MULTIHORMONAL PANCREATIC TUMOR.

Keller U, Fankhauser S, Schumacher A, Trimble ER, Heitz PU

Departement innere Medizin, Abteilung Endokrinologie und Stoffwechsel, Kantonsspital, CH-4031 Basel, Switzerland

Schweiz Med Wochenschr; 112(9):297-303 1982

A 60-yr-old patient developed signs and symptoms of glucagonoma syndrome (dermatitis, wt loss, anemia and hypoaminoacidemia). However, diabetes mellitus was absent. Glucagonoma was suspected because of markedly elevated plasma glucagon levels and the tumor was subsequently removed by surgery. Acidethanol extraction of the tumor and immunohistochemistry provided evidence of the presence of all four islet hormones, particularly that of glucagon and pancreatic polypeptide and to a lesser extent of somatostatin and insulin. Immunohistochemistry of the tumor (but not plasma) also showed the presence of alpha-HCG. Plasma glucagon immunoreactivity consisted to a large extent (approx 90%) of a high molecular form of glucagon, probably proglucagon. In spite of the presence of alpha-HCG - which is assumed to be a marker of malignancy - the patient had been free of recurrence for the 2-1/2 yr since surgery. The increasing number of cases reported during the past few yr demonstrates that the syndrome is more common than previously suspected. Glucagon secretion and its typical clinical picture may be a valuable marker of a multihormonal pancreatic tumor. In a case of suspected glucagonoma, diagnosis can be established simply by obtaining a plasma glucagon level measurement. (Author abstract) (16 Refs) (In GER)

33. HYPOGLYCEMIC PERIPHERAL NEUROPATHY IN ASSOCIATION WITH INSULINOMA: IMPLICATION OF GLUCOPENIA RATHER THAN HYPERINSULINISM. CASE REPORT AND LITERATURE REVIEW.

Jaspan JB, Wollman RL, Bernstein L, Rubenstein AH

Dept. Medicine, Section Endocrinology, Univ. Chicago, Pritzker Sch. Medicine, 950 East 59th St., Chicago, IL, 60637

Medicine (Baltimore); 61(1):33-44 1982

A syndrome of peripheral polyneuropathy associated with islet cell tumors and hypoglycemia has been reported in 28 patients. Despite varying features in these patients, the clinical characteristics of this syndrome are remarkably similar. These consist of the development of a sensorimotor neuropathy during a protracted course of recurrent severe hypoglycemia, related to underlying insulinoma. Cerebral symptoms dominate the clinical picture and a predominantly or entirely motor, distal and symmetric, peripheral neuropathy ensues. Upper limb involvement is more frequent, accompanied by severe weakness and distal wasting, usually without fasciculations. Painful distal paresthesias without objective sensory loss are characteristic. Direct relationship to a single hypoglycemic insult is often absent. This report describes the clinical features and laboratory investigation of a new case with this condition, reviews the literature and discusses the syndrome with special regard to the etiology. (Author abstract) (31 Refs)

34. TUMORS OF THE ENDOCRINE PANCREAS.

Friesen SR

Dept. Surgery, Univ. Kansas Medical Center, Kansas City, KS, 66103

N Engl J Med; 306(10):580-590 1982

Pancreatic endocrinopathies are discussed with respect to the formulation of the amine-precursor uptake and decarboxylation (APUD) concept, the study of evolution of pathogenetic types of APUD-cell dysplasias, advances in diagnosis and tumor localization, new therapeutic methods, and the clinical recognition of syndromes. Ectopic pancreatic endocrine tumors described include glucagonoma (diabetes-dermatitis syndrome), pancreatic polypeptide islet-cell tumor, and carcinoid tumor of the pancreas (atypical carcinoid syndrome). Ectopic endocrine tumors of the pancreas include pancreatic gastrinoma (ectopic ulcerogenic syndrome), vipoma of the pancreas (watery-diarrhea syndrome), pancreatic corticotropinoma (ectopic-ACTH syndrome), and others. Diagnosis of these pancreatic tumors has been improved with recent developments in the quantitative measurement of circulating polypeptide hormones and in the cytochemical identification of APUD-cell tumors. (108 Refs)

35. STATEMENT ON HYPOGLYCEMIA.

Rizza RA, Gerich JE

American Diabetes Association., 2 Park Avenue, New York, NY, 10016

Diabetes Care; 5(1):72-73 1982

Causes and treatment of hypoglycemia (HG) are discussed. Treatment depends upon whether the disorder is reactive (fed) or fasting HG. Fasting HG can be caused by pancreatic tumors composed of B-cells of the islets of Langerhans. HG can be a symptom of adrenal and pituitary insufficiency, while these conditions rarely cause HG. Under certain circumstances, alcohol, pills used to treat diabetes, and salicylates can cause fasting HG. (no Refs)

GONADAL TUMORS

36. GONADAL DYSGENESIS WITH KARYOTYPE 46 XY IN TWO SISTERS EACH WITH A NON-RUDIMENTARY GONAD WITHOUT HISTOLOGICAL EVIDENCE OF GONADOBLASTOMA. DEMONSTRATIONS OF SECRETION OF ANDROGENS BY ONE OF THESE GONADS.

Cuvelier-Trio C, Le Capon JB, Gasnault JP, Desmons F, Buvat J, Netter, Belaisch

Service de gynecologie, C.H.U. Lille, Avenue Oscar Lambert, F59000 Lille, France

Gynecologie; 32(3):297-303 1981

Gonadal dysgenesis with karyotype 46 XY was diagnosed in two sister (21 and 25 yr old) who had gonads which were nearly normal in vol, did not correspond to gonadoblastomas, but were capable of secreting androgens. Serum estradiol was low while serum androgens were normal. A clear gradient of secretion for androstenedione, testosterone, and 17-OH-progesterone was evident in hormonal assays of blood from the efferent gonadal vein. (25 Refs) (In FRE)

37. ALTERATIONS IN THYROID HORMONE METABOLISM DURING CHEMOTHERAPY IN PATIENTS WITH TESTICULAR CARCINOMA.

Willemse PH, Sleijfer DT, Sluiter WJ, Schraffordt Koops H, Doorenbos H

Dept. Endocrinology, Internal Medicine, Univ. Hosp., Oostersingel 59, 9713 EZ Groningen, The Netherlands

Clin Endocrinol (Oxf); 16(3):303-313 1982

In a prospective study, the effects of chemotherapy on thyroid function in patients with non-seminoma testicular carcinoma were evaluated. Thirty-one patients were studied; in 16 immunoassayable HCG was present, but altered thyroid function could not be established. In 15 patients an exaggerated TSH response to TRH was observed. In these patients, although T3 and T4N values were normal, basal TSH levels were higher compared to patients with a normal TSH response, probably due to preceding lymphangiography. During chemotherapy, T4N, T3 and rT3 levels rose significantly, but basal TSH levels and the TSH response to TRH decreased. In contrast, the prolactin responses to TRH increased. The observed changes in thyroid function during chemotherapy appear to result from delayed thyroid hormone clearance, probably caused by an effect o f chemotherapy on deiodinating enzyme activity. This would result, in an increase in T4N and rT3 levels and a fall in TSH levels and in the TSH response to TRH. Furthermore, after therapy the raised T4N and lowered TSH levels remained, whilst the FT3 level did not change either during or after therapy, suggesting an unaltered hypothalamic/pituitary axis. (Author abstract) (43 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

38. STEROID RECEPTORS IN EARLY BREAST CANCER: VALUE IN PROGNOSIS.

Nicholson RI, Campbell FC, Blamey RW, Elston CW, George D, Griffiths K
Tenovus Inst. Cancer Res., Cardiff, Wales
J Steroid Biochem; 15:193-199 1981

The relationship of prognosis to estradiol-17 beta receptor (ER)-status of primary breast tumors was studied in 550 patients who presented consecutively to one surgeon (Group A) and in 421 patients dealt with by 15 surgeons (Group B). Systemic treatment of patients after mastectomy was withheld until recurrence of disease. Clinical staging of Group A was by node involvement, and Group B by the international TNM system. Data from both groups indicate no relationship between ER-status and the stage of the disease, nor with tumor size. No advantage is evident by considering the quantity of receptor in the primary tumor since the correlations are not sufficiently strong to allow the prediction of recurrence to be accurately assessed for an individual patient. Group A patients with nodal involvement and ER-positive tumors have, as a group, a more favorable prognosis, approx 70% surviving 3 yr. Node positive ER-positive patients with grade I and II tumors have a good prognosis and do as well as patients without nodal involvement. Tumors with measurable receptor levels were found in 219 patients of Group B. A group of 116 patients without nodal involvement but with ER-negative tumors, despite favorable prognosis, unexpectedly recurred at the same rate as all women with axillary node involvement. Generally the rate of survival was significantly longer in patients with ER-positive tumors. In Group A major local recurrence occurred in 82 patients of whom 42 developed distant metastases and a further 82 had clinical evidence of distant metastases without prior local recurrence. ER-status did not relate to local recurrence, nor to the incidence of 'spot' recurrence. Thirty-one percent of Group A patients with ER-positive primary tumors treated with endocrine therapy responded, while only 5% of the ER-negative tumors were confirmed as responders by external assessment. (30 Refs)

39. ESTROGEN RECEPTOR ASSAYS IN FAMILIAL AND NONFAMILIAL BREAST CANCER.

Ottman R, Hoffman PG, Siiteri PK, Korenman SG
G. H. Sergievsky Center, Faculty Medicine, Columbia Univ., 630 West 168th St., New York, NY, 10032
Banbury Rep; 8:197-211 1981

Familial and nonfamilial breast cancer was compared with respect to the binding capacity (ER) and dissociation constant (KD) of the estrogen receptor. ER content of breast cancer tissue was influenced by the hormonal environment in which the tumor had grown and by tumor pathology. Elevated KD values observed in familial breast cancer may reflect an underlying endocrine abnormality which resulted in the development of breast cancer. Tissue estrogen concentrations may be higher in familial than nonfamilial breast cancer, and some of the variation in ER and KD may be explained by genetically determined differences in endocrine factors that relate to susceptibility to breast cancer. (12 Refs)

40. ENDOCRINE THERAPY OF BREAST CANCER PATIENTS.

Basaalyk LS, Murav'eva NI, Smirnova KD, Kuz'mina ZV
Lab. Clinical Biochemistry, Cancer Res. Center, Moscow, USSR
Sov Med; (12):54-59 1981

Physiological principles of the therapeutic effect of steroid hormones and the role of steroid receptors in the growth and regression of breast cancer were reviewed. Determination of the level of estrogen receptors (ER) showed that 55-60% of ER-positive breast tumors responded to the endocrine therapy. The patients with ER-negative tumors had a significantly greater incidence of recurrence. It was shown that simultaneous determination of ER and progesterone receptors (PR) enhances the accuracy of prognosis of tumor response to hormone therapy. Recent data on the presence of glucocorticoid and androgen receptors indicate that these receptors play a certain role in tumor response to glucocorticoids and androgens. (63 Refs) (In RUS)

41. REPRODUCTIVE ENDOCRINOLOGY AND BREAST CANCER IN WOMEN.

Korenman SG, Lippman, Zumoff, Pike MC, Segaloff
Dept. Medicine, Univ. of California Los Angeles-San Fernando Valley Program, VA Medical Center, Sepulveda, CA, 91343
Banbury Rep; 8:71-85 1981

Normal and abnormal reproductive functions were studied focusing on the regulation of the mammary gland by the principal reproductive hormones. Interactions between estrogens, progesterone, prolactin, and conditions of estrogen excess or unopposed estrogens are presented. Because of lack of moment-by-moment assessment of the endocrine status of the breast, complex endocrine interrelations characterizing normal and abnormal reproductive cycles affecting the breast were considered only theoretically. (61 Refs)

42. A PROSPECTIVE STUDY OF THE RELATION BETWEEN THYROID FUNCTION AND SUBSEQUENT BREAST CANCER.

Bulbrook RD, Thomas BS, Fantl VE, Hayward JL, Lippman M, Siiteri PK, Korenman SG
Dept. Clinical Endocrinology, Imperial Cancer Res. Fund, London WC2A 3PX, England
Banbury Rep; 8:131-141 1981

Prospective studies of 5,000 normal women were conducted to investigate the relationship between thyroid function and the development of breast cancer. Up to the age of 45 yr, thyroid dysfunction was not correlated to increased risk by women with a positive family history of breast cancer and was of no etiologic significance in the precancer group. In peri- and postmenopausal women with hypothyroidism, the thyroid gland appears to be involved in the development of breast cancer. (18 Refs)

43. BREAST CANCER: DIET AND HORMONE METABOLISM.

Hill P, Garbaczewski L, Kasumi F, Kuno K, Helman P, Wynder EL, Topp W, Pike MC, Henderson BE, Segaloff A, Sirbasku DA, Korenman SG, Cole P, Zumoff B
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Banbury Rep; 8:257-277 1981

The effect of diet modification on hormonal metabolism of women at low risk (black South African and Japanese) and women at high risk (North American caucasian) for breast cancer was investigated. Differences in the hormonal profile during the menstrual cycle between the three races of women were noted. Differences in pituitary response in circulating hormone levels and in duration of menstrual cycle occurred when a Western diet was interchanged for a vegetarian diet, and vice versa. The therapeutic value of this observation is unknown. (94 Refs)

44. HORMONES AND BREAST CANCER.

Pike MC, Siiteri PK, Welsch CW
Dept. Family and Preventive Medicine, Univ. Southern California Sch. Medicine, Los Angeles, CA, 90033
Banbury Rep 8: 491 pp., 1981.

Sessions held to discuss the relationship between hormones and breast cancer (BC) consisted of the following topics: review of BC epidemiology (as it relates to menarche, pregnancy, and menopause, body size and BC risk), endocrinology of women at risk of BC (hormone profiles in young women at risk of BC with analysis of ovarian function during theelarche, menarche, and menopause, and after childbirth, endocrine maturation during female puberty, reproductive endocrinology and BC in women, increased availability of serum estrogens in BC), review of studies attempting to establish endogenous hormones as important in human BC (estrogens, progesterone, and prolactin in human BC, prospective study of relation between thyroid function and BC, and abnormal plasma hormone levels in women with BC), in vitro studies of human breast tissue (hormonal regulation of human BC cells in vitro, prolactin, pituitary hormones, and BC, estrogen receptor assays in familial and nonfamilial BC), exogenous hormones and BC (epidemiological studies of the role of exogenous estrogens in BC etiology and hormone therapy), other exogenous factors and BC (epidemiological studies of mutagenicity of breast fluids and BC risk, diet and hormone metabolism in BC), hormones and genesis of progression of murine mammary tumors (ovarian steroid hormones, prolactin, growth hormone, insulin, pituitary and steroid hormones, pregnancy and lactation, neuroleptic drugs, and plasma pro lactin analysis), and mechanism of hormone action (regulation of casein gene expression in hormone-dependent mammary cancer, control of estrogen-responsive tumor growth, and role of hormones in mammogenesis and carcinogenesis). (453 Refs)

45. HORMONAL PATTERN IN PROSTATIC CANCER. II. CORRELATION WITH PRIMARY RESPONSE TO ENDOCRINE TREATMENT.

Adlercreutz H, Rannikko S, Kairento AL, Karonen SL
II Dept. Surgery and Dept. Clinical Chemistry, Univ. Helsinki, Helsinki, Finland
Acta Endocrinol (Copenh); 98(4):634-640 1981

In 32 subjects with histologically and/or cytologically verified prostatic cancer the hormonal pattern was studied by assaying 18 plasma and urinary hormones or groups of hormones and relating the values to the response to endocrine treatment. Total orchidectomy (orchiepididymectomy) was performed on 9 patients, subcapsular orchidectomy on 13 patients and estrogen therapy with Estradurin was given in 4 patients. Six patients had total orchidectomy followed by estrogen therapy. With few exceptions all values were within the normal range. The only significant exceptions were the high urinary estrogen values and the low urinary estrone estradiol-estriol ratio observed as compared to healthy males working in a factory. No urinary hormone values or ratios of hormone values could be used for the prediction of prognosis in prostatic carcinoma patients. However, the ratios of plasma testosterone/estradiol (T/Oe2) and testosterone/prolactin (T/Prl) were found to give good information with regard to the response to endocrine treatment. High values for one or both of these ratios meant a good response to treatment in all subjects without exception in this material. Subjects with both ratios low had a good response to endocrine treatment in 50% of the cases. No other plasma hormones measured were of any help prognostically. It is concluded that by measuring the T/Oe2 and T/Prl ratios it seems possible to select a group of patients with favorable primary response to endocrine treatment. (Author abstract) (27 Refs)

46. THE IMMUNOCYTOCHEMICAL DETECTION OF PROTEIN HORMONES IN HUMAN PROSTATIC TISSUES.

Sibley PE, Harper ME, Peeling WB, Joyce BG, Griffiths K
Tenovus Inst. for Cancer Res., The Heath, Cardiff CF4 4XX, Wales
Prostate; 2(2):175-185 1981

Benign prostatic hyperplastic tissue was obtained from 13 patients, and immunocytochemical detection of four pituitary protein hormones was investigated. Luteinizing hormone (LH), follicle stimulating hormone (FSH), growth hormone (GH), and prolactin were measured. In all 13 specimens, a minimal amount of staining was observed when the LH antiserum was used in the immunocytochemical process. Diffuse staining was observed in both stromal and epithelial regions and an artefactual precipitate was found above the plane of the section, making it difficult to estimate the significance of the results. Staining attributable to FSH antiserum was observed in cytoplasm of epithelial cells lining acini and in their secretions. Most cystic acini were intensely stained, while only a proportion of the epithelium in glandular acini displayed immunoreactive FSH localization. Stromal areas were blank. With GH antiserum, staining was confined to stromal areas and the epithelium was predominantly unstained. Prolactin was localized intracellularly in most of the epithelial cells. These results are consistent with the internalization of fragments or whole protein hormone molecules in prostatic epithelium; their significance is unclear. (33 Refs)

47. THE BIOCHEMICAL PROPERTIES OF URINARY HUMAN CHORIONIC GONADOTROPIN FROM THE PATIENTS WITH TROPHOBLASTIC DISEASES.

Nishimura R, Endo Y, Tanabe K, Ashitaka Y, Tojo S
Dept. Obstetrics and Gynecology, Kobe Univ. Sch. Medicine, Kobe 650, Japan
J Endocrinol Invest; 4(3):349-358 1981

Human chorionic gonadotropin (hCG) was extracted from urine of a 23-yr-old woman with a hydatidiform mole, a 37-yr-old woman with metastatic choriocarcinoma, and a woman with a normal pregnancy by the standard kaolin-acetate method in conjunction with alcohol precipitation. Purification by diethylaminoethyl-cellulose chromatography and Sephadex G-100 gel filtration was followed by determination of amino acids, carbohydrates, and monosaccharides, sodium dodecyl sulfate polyacrylamide gel electrophoresis, 125I-hCG radioimmunoassay, 125I-hCG uptake in rats, and bioassay by ovarian wt method. Amino acid compositions of the three hCG samples were virtually identical. All three types of hCG could be separated into alpha and beta components by electrophoresis. They were similar in cross reactivities in terms of parallel dose response and dose inhibition to each other in hCG, alpha, and beta-subunits radioimmunoassays. The sialic acid content of hCG from the choriocarcinoma patient was undetectable, whereas the other two hCGs had about 8.5% sialic acid. Ovarian uptake of 125-hCG from the choriocarcinoma patient was approx 10% of the uptakes of the other two 125-hCG types, and agrees with low biological activity determined by the rat ovarian wt assay. Neoplastic or malignant transformation of trophoblasts may alter glycosylation, especially sialylation. (46 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

48. COMPARISON OF TWO PARENTERAL DIPHOSPHONATES IN HYPERCALCEMIA OF MALIGNANCY.

Jung A
Dept. Medicine, Univ. Hosp., Geneva, Switzerland
Am J Med; 72(2):221-226 1982

The two diphosphonates, ethane-hydroxy-diphosphonate (EHDP) and dichloromethylene-diphosphonate (Cl2MDP) were injected into 30 patients with one or multiple episodes of hypercalcemia caused by osteolytic metastases. All patients responded well to the treatment after a mean delay of two days. Cl2MDP was slightly more efficient than EHDP, but there was no difference in serum calcium measured after 5 days of therapy with Cl2MDP or after 10 days of EHDP: in both cases, the calcium level was normal. No acute or long-term side effect has been observed. Parenteral diphosphonates may well be the treatment of first choice against malignant hypercalcemia. (Author abstract) (15 Refs)

49. RECENT ADVANCES IN PARATHYROID HORMONE RESEARCH.

Habener JF
Lab. Molecular Endocrinology, Massachusetts General Hosp., Harvard Medical Sch., Boston, MA, 02114
Clin Biochem; 14(5):223-229 1981

The introduction of blood calcium determinations as part of routine health screening procedures in this country has led to the discovery of a much higher incidence of primary hyperparathyroidism than was recognized previously. Research efforts have focused on studies of the cellular defects in the regulation of parathyroid hormone biosynthesis and secretion that are characteristically found in adenomatous and hyperplastic parathyroid glands. The available evidence indicates that the secretory defect probably resides at two levels; (1) a defect in the calcium sensor of the abnormal glands ('set-point' error) and (2) an exaggeration of a small component of autonomous hormone secretion that becomes relevant due to the large mass of glandular tissue. Regulation of parathyroid hormone synthesis appears to be at the level of cell replication (hyperplasia) and at the level of intracellular turnover of hormone. Marked heterogeneity of hormone in the circulation arises as a result of both glandular and extraglandular cleavages of hormone and the predominant circulating form of the hormone are biologically inactive, COOH-terminal fragments. Because most cases of hypercalcemia that accompany cancer are caused by humoral substances other than parathyroid hormone, sensitive radioimmunoassays that detect COOH-terminal fragments should distinguish patients with hypercalcemia due to cancer from those with primary hyperparathyroidism. (Author abstract) (35 Refs)

50. HYPOPARATHYROIDISM AND HYPOCALCAEMIA DURING TREATMENT FOR ACUTE LEUKAEMIA.

Freedman DB, Shannon M, Dandona P, Prentice HG, Hoffbrand AV
Metabolic Unit, Dept. Chemical Pathology, Royal Free Hosp. and Sch. Medicine, London NW3 2QG, England
Br Med J; 284(6317):700-702 1982

Nine patients with acute leukemia developed a complex syndrome of hypocalcemia and hypomagnesemia during treatment. These metabolic abnormalities developed rapidly in some patients and gave rise to acute symptoms. Immunoreactive parathormone concentrations in these patients were found to be either absolutely or inappropriately low. Hypomagnesemia and the action of chemotherapeutic agents, especially adriamycin or cytarabine, or both may have contributed to the pathogenesis of this syndrome. (Author abstract) (10 Refs)

51. PRIMARY HYPERPARATHYROIDISM IN CHILDREN.

Girard RM, Belanger A, Hazel B
5415, boul. de l'Assomption, Montreal, PQ H1T 2M4, Canada
Can J Surg; 25(1):11-13,32 1982

Primary hyperparathyroidism is rare in children. This report describes a 15-yr-old boy who had an intrathymic chief cell adenoma. The literature related to this condition in neonates and children is reviewed. Neonatal hyperparathyroidism differs from hyperparathyroidism in children. The severity of symptoms and osseous lesions, genetic inheritance in many, pathological changes in the parathyroid glands and the need for more extensive treatment in neonates and infants indicate that primary hyperparathyroidism in these patients should be considered as a different entity from that occurring in older children. (Author abstract) (32 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

52. THE PATTERN OF ECTOPIC HORMONE PRODUCTION IN LUNG CANCER.

Bondy PK
West Haven Veterans Admin. Medical Center, West Haven, CT, 06516
Yale J Biol Med; 54(3):181-185 1981

Pulmonary cancers produce many hormonal polypeptides. There is a tumor-specific pattern to the appearance of abnormal adrenal function and inappropriate secretion of vasopressin, which are frequently found in small cell undifferentiated carcinoma but occur only very rarely, if at all, in squamous tumors. Humoral hypercalcemia, on the other hand, occurs almost entirely in squamous tumors and is rarely if ever seen in small cell or large cell tumors or in adenocarcinoma. In contrast, 'big ACTH' and beta lipotropin are found in the plasma and tumor extracts of lung cancers of all types. Calcitonin and the beta chain of human chorionic gonadotropin are also found in the plasma of a considerable portion of patients with all histological types of lung cancers. (Author abstract) (29 Refs)

53. CARCINOMA OF THE LUNG WITH MARKED HYPERAMYLASEMIA AND ELEVATED SERUM CALCITONIN.

Roberts I, Chopra S, Warshaw AL
(c/o Chorpa) Gastroenterology Section, West Roxbury Veterans Admin., Medical Center, 1400 VFW Parkway, West Roxbury, MA, 02132
Am J Gastroenterol; 77(1):43-44 1982

Ectopic production of multiple peptide hormones is a frequent concomitant of neoplasia. An elderly man with metastatic small cell carcinoma of the lung presented with back pain, a right hilar mass, and was demonstrated to have markedly elevated serum calcitonin and amylase levels. Polyacrylamide gel electrophoresis revealed a striking elevation of a 'salivary type' isoamylase. We report this case as an unusual association of production of both a peptide hormone and a nonhormonal peptide in a patient with a tumor of 'neural crest' origin. (Author abstract) (15 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

54. RADIOIMMUNOASSAY DETECTION OF ENDORPHINS FROM LONG-TERM CULTURE OF HUMAN PITUITARY TUMOUR CELLS.

Sharp B, Melmed S, Goldberg R, Carlson HE, Refetoff S, Hershman JM
(c/o J. Sinadinovic) Endocrinological Lab., INEP, P. O. Box 46, YU-11080 Zemun, Yugoslavia
Acta Endocrinol (Copenh); 99(2):174-178 1982

Using a sensitive and precise radioimmunoassay for human beta-endorphin, we have demonstrated the sustained secretion of opioid peptides from human pituitary tumor cells. Pituitary tumor tissue obtained from a patient with Nelson's syndrome was maintained in continuous monolayer culture and secreted both beta-lipotropin and beta-endorphin, with predominance of the latter. This is compatible with the idea that the beta-endorphin in normal human serum is secreted as such despite the predominance of beta-lipotropin compared with beta-endorphin in the anterior pituitary. (Author abstract) (14 Refs)

55. PROOPIOLIPOMELANOCORTIN PEPTIDES IN NORMAL PITUITARY, PITUITARY TUMOR, AND PLASMA OF NORMAL AND CUSHING'S HORSES.

Wilson MG, Nicholson WE, Holscher MA, Sherrell BJ, Mount CD, Orth DN
(c/o Orth) Div. Endocrinology, A-4215 Vanderbilt Medical Center North, Nashville, TN, 37232
Endocrinology; 110(3):941-954 1982

Using RIAs for six regions within proopiolipomelanocortin (proOLMC), gel filtration, and electrophoresis, we studied pituitary peptides in a normal horse and one with Cushing's disease caused by a pars intermedia adenoma. Almost all immunoreactive (IR) ACTH (78%) was 4,500 mol wt (4.5K) ACTH in normal pars distalis, but it was almost 100% corticotropin-like intermediate lobe peptide (CLIP) in normal pars intermedia. alphaMSH and betaMSH were found mainly in pars intermedia; equal concentrations of the betaMSH precursors, betalipotropin (betaLPH) and gammaLPH, were found in pars distalis. Most IR-beta-endorphin (IR-betaEND) was found as betaEND in pars intermedia, but roughly equal concentrations of betaEND and its precursor, betaLPH, were found in pars distalis. A 33K molecule containing IR-ACTH, IR-gamma3MSH, and IR-betaEND, presumed to be proOLMC, and a variety of 15-27K presumed biosynthetic intermediates were found in both normal pars distalis and pars intermedia. The pars intermedia adenoma causing Cushing's syndrome contained high IR-peptide concentrations. Several differences in precursors were noted, including the presence of three larger presumed precursors (38.5K, 47K, and 63K) that had both ACTH and betaEND immunoreactivities and both deletions and additions of 15-27K intermediates. The Cushing's horse's plasma peptides reflected tumor concentrations; 4.5K ACTH was modestly elevated, but the concentrations of CLIP, alphaMSH, betaMSH, gammaLPH, and betaEND were dramatically increased. About 20% of plasma IR-ACTH and 5% of IR-betaMSH and IR-betaEND were found as high mol wt forms. Normal processing of horse proOLMC appears to be similar to that in other species, but may be altered in pars intermedia tumors of horses with Cushing's disease, the plasma of which contains disproportionately increased concentrations of pars intermedia proOLMC peptides. (Author abstract) (51 Refs)

56. EVIDENCE THAT STIMULATION OF THYROTROPIN AND PROLACTIN SECRETION BY THYROTROPIN-RELEASING HORMONE OCCUR VIA DIFFERENT CALCIUM-MEDIATED MECHANISMS: STUDIES WITH VERAPAMIL.

Geras E, Rebecchi MJ, Gershengorn MC
(c/o Gershengorn) Dept. Medicine, C-D Bellevue, New York Univ. Medical Center, 550 First Ave., New York, NY, 10016
Endocrinology; 110(3):901-906 1982

TRH stimulation of TSH and PRL secretion requires Ca. We determined whether influx of extracellular Ca was involved in TRH action in TtT cells (mouse pituitary tumor cells in short term culture that produce TSH), in GH3 cells (clonal rat pituitary tumor cells that produce PRL), and in anterior pituitary cells in vitro derived from normal rats. TRH increased 45Ca uptake by TtT cells by 40% but had no effect on 45Ca uptake by GH3 cells. Verapamil, which totally inhibited 45Ca uptake by TtT and GH3 cells induced by depolarization with 50 mM K, was employed to block influx of extracellular Ca. Verapamil (50 uM) abolished the increment in 45Ca uptake by TtT cells caused by TRH. Verapamil had no effect on TRH-stimulated 45Ca efflux and PRL release from GH3 cells but partially inhibited TRH-stimulated 45Ca efflux and TSH release from TtT cells during perifusion. TRH-stimulated PRL release from GH3 cells was likewise not affected by verapamil during static incubation (7.2 -1.1 ng/ml vs 6.2 -1.2 ng), but TRH-stimulated TSH release from TtT cells was inhibited by 64% (from 5.5 -0.7 ngeq/ml to 2.0 -0.6 ngeq). Similar findings on the effects of verapamil on hormone release were obtained from nonneoplastic anterior pituitary cells; TRH-stimulated PRL release was not affected, but TRH-stimulated TSH release was inhibited by 50%. Hence, TRH did not cause Ca influx into mammotropic cells and TRH-stimulated PRL release was not affected when Ca influx was blocked by verapamil. In contrast, TRH appeared to cause Ca influx into thyrotropic cells, and TRH-stimulated TSH release was partially inhibited when Ca influx was blocked by verapamil. We suggest that TRH action in mammotrophs involves only mobilization of cellular Ca, whereas TRH action in thyrotrophs involves mobilization of cellular Ca and influx of extracellular Ca. (Author abstract) (29 Refs)

57. INHIBITION BY 17BETA-ESTRADIOL OF THE GROWTH OF THE RAT PITUITARY TRANSPLANTABLE TUMOR MTF4.

Morel Y, Albaladejo V, Bouvier J, Andre J
(c/o Andre) Laboratoire Biochimie Endocrinienne, UER Lyon-Nord, Hopital Debrousse, 29 Rue Soeur Bouvier, 69322 Lyon Cedex 1, France

Cancer Res; 42(4):1492-1497 1982

The effects of pharmacological doses of estradiol on the growth of the rat pituitary transplantable tumor MtF4 have been characterized. After sc injection into control rats of a cell suspension prepared from the tumor, in 12 experiments, the av range of days when a new tumor became palpable was between 14.7 -2.3 (SD) and 24.5 -3.3. rats. Daily im injections of 10 ug 17beta-estradiol benzoate or 17beta-estradiol implanted in Silastic tubing partially inhibited the tumor growth as judged by the wt and the time of appearance of the tumor. The same treatments increased the pituitary wt. Both effects were dose dependent above 3 ug 17beta-estradiol benzoate per day and displayed some specificity. 17alpha-Estradiol did not modify the pituitary or the tumor growth significantly; 17beta-hydroxy-3-keto-5alpha-androstane also did not modify the tumor growth. The inhibitory effect of 17beta-estradiol on tumor growth has also been observed in hypophysectomized rats. The tumor cytosol contained 30 to 220 fmol of specific estrogen-binding sites per mg protein which were characterized by: a high affinity (Kd, 0.25 to 0.65 x 10-9M); a sedimentation constant of 6 to 8S; and their hormone specificity. Thus, 17alpha-estradiol, which was inactive in vivo, had an affinity only fourfold lower than 17beta-estradiol. We conclude that pharmacological doses of 17beta-estradiol inhibit in a dose-dependent manner and with some specificity the growth of the MtF4 transplantable pituitary tumor while increasing the growth of pituitary. We suggest this inhibition requires estrogen receptors and is not mediated via the pituitary, but we cannot specify whether this inhibition was direct or not. (31 Refs)

58. SOMATOSTATIN-28 ENCODED IN A CLONED CDNA OBTAINED FROM A RAT MEDULLARY THYROID CARCINOMA.

Goodman RH, Jacobs JW, Dee PC, Habener JF
Lab. Molecular Endocrinology, Massachusetts General Hosp., Boston, MA, 02114

J Biol Chem; 257(3):1156-1159 1982

We have constructed and cloned in bacteria complementary DNAs derived from a transplantable rat medullary thyroid carcinoma. Using a hybridization probe encoding an anglerfish islet pre-prosomatostatin, a precursor of the tetradecapeptide somatostatin, we have identified and isolated a clone containing a 400-base pair complementary DNA encoding most of the rat carcinoma pre-prosomatostatin. The amino acid sequence of the tetradecapeptide somatostatin and of the amino-terminally extended form, somatostatin-28 was deduced from the nucleotide sequence of the complementary DNA. Somatostatin-28 was found at the COOH terminus of a polypeptide of at least 80 amino acids indicating that somatostatin-28 arises by cleavage from a large precursor. The sequences of somatostatin-28 and somatostatin-14 are strictly conserved between the rat and other mammals. Such conservation of these sequences indicates strong selective pressures during evolution to maintain the sequence and suggests that somatostatin-28 may serve some essential biologic functions apart from, or in addition to, the important regulatory actions of somatostatin-14. Additionally, we found a high degree of homology in the amino acid sequences of the NH2-terminal extension peptides in the anglerfish islet and the rat carcinoma pre-prosomatostatins pointing further to a possible biologic function of these extension peptides. (Author abstract) (39 Refs)

59. SPECIFIC HIGH AFFINITY BINDING SITES FOR SOMATOSTATIN-28 ON PANCREATIC BETA-CELLS: DIFFERENCES WITH BRAIN SOMATOSTATIN RECEPTORS.

Reubi JC, Rivier J, Perrin M, Brown M, Vale W
Peptide Biology Lab., Salk Inst., P.O. Box 85800, San Diego, CA, 92138

Endocrinology; 110(3):1049-1051 1982

Saturable and high affinity binding sites have been obtained for an iodinated somatostatin-28 (SS-28) analog, [Leu8,D-Trp22,125I-Tyr25] SS-28, in a membrane preparation from hamster insulinoma, mainly composed of pancreatic beta-cells. Specific binding is maximal after 1 hr incubation at 22 C and represents 65% of the total binding. KD for [Leu8,D-Trp22,Tyr25] SS-28 is 0.25 nM with the number of sites corresponding to 68 fmol/mg protein. The Kd for SS-28 (1 nM) is more than 5 times lower than that for SS-14. SS-28 analogs, such as [D-Trp22] SS-28 and analogs which selectively inhibit insulin release in vivo (Des-Asn5[D-Trp8,D-Ser13] SS-14 and Des-Asn19[D-Trp22,D-Ser27] SS-28), are the most potent compounds in this assay. C-terminal replacement of L-cysteine by D-cysteine reduces the apparent affinity of SS analogs. Unrelated peptides and the inactive analog Des-Trp8-SS-14 have no affinity for insulinoma binding sites. There are differences between the insulinoma SS binding sites and those monitored under similar conditions from rat cerebral cortex. In cerebral cortex, SS-14 and SS-28 have similar affinity for the binding sites, and the insulin selective analogs are less potent than SS-14. It is concluded that pancreatic beta-cells, as well as brain, possess high affinity binding sites for SS, but that they differ in some of their pharmacological properties. (Author abstract) (16 Refs)

60. HORMONAL REGULATION OF HUMAN BREAST CANCER CELLS IN VITRO.

Lippman M, Meites J, Welsch CW, Rosen JM, Segaloff A, Korenman SG, Nandi S, Sirbasku DA
Medical Breast Cancer Section, Medicine Branch, NCI, Bethesda, MD, 20205

Banbury Rep; 8:171-184 1981

Cultured breast cancer cell lines (most of which were derived from neoplastic effusions, often after treatment) differ from the original tumors in several important ways. Experiments with these cell lines must be designed and their results interpreted with great caution. Firm conclusions as to the absence of a given hormone response are particularly difficult to interpret. Positive results are much less ambiguous, but these can also give rise to misinterpretations. Nevertheless, the cell-culture approach provides several advantages in the investigation of hormonal interactions with human breast cancer. In particular, drug- and hormone-resistant variants of wild-type parental cell lines can be used to study the mechanisms of hormone dependence. Hormones now known to affect the growth or differentiated functions of human breast cancer cells (especially the MCF-7 cell line) include estrogens, glucocorticoids, androgens, thyroid hormones (the ZR-75-1 cell line is absolutely dependent on physiologic levels of triiodothyronine in the medium, and MCF-7 cells are also thyroid hormone dependent), and insulin. Vitamin A derivatives are required for normal epithelial differentiated and inhibit several types of chemical carcinogenesis in rats. Several human breast cancer cell lines contain separable binding activities for retinol and retinoic acid, but clinical trials of 13-cis-retinoic acid in breast cancer patients have not been encouraging. The roles of epidermal growth factor, vitamin D, progesterone, and prolactin in breast cancer growth are not yet clear. (46 Refs)

61. PROSTATE CARCINOMA TUMOR SIZE IN RATS DECREASES AFTER ADMINISTRATION OF ANTAGONISTS OF LUTEINIZING HORMONE-RELEASING HORMONE.

Redding TW, Coy DH, Schally AV
Endocrine and Polypeptide Lab., Veterans Admin. Medical Center, New Orleans, LA, 70146
Proc Natl Acad Sci USA; 79(4,part1):1273-1276 1982

The effects of two potent antagonistic analogues of luteinizing hormone-releasing hormone (LH-RH) on the growth of two different models of rat prostate tumors have been investigated. Chronic administration of [NAc-p-F-DPhe1,p-Cl-DPhe2,DTrp3,6,D-Ala(10)]LH-RH (antagonist I) at 50 ug/day for 21 days significantly inhibited the growth of the chemical induced squamous cell carcinoma 11095 in Fischer 344 male rats. The weights of the pituitary, ventral prostate, and testes were not significantly altered. After 21 days of treatment with this analogue, serum luteinizing hormone (lutropin), follicle-stimulating hormone, and testosterone levels were markedly decreased. When male Copenhagen F-1 rats bearing the Dunning 3327H prostate adenocarcinoma were injected with antagonist I at 50 ug/day for 6 wk or with [NAc-p-Cl-DPhe1,2,DTrp3,DPhe6,DAla(10)]LH-RH (antagonist II) at 50 ug/day for 17 days, the percentage increase in tumor volume was decreased to half or less and the actual tumor volume was diminished 34-96% compared to controls. Tumor weight was decreased 30% and 89% after antagonist I and II, respectively, compared to untreated controls. The tumor doubling time was 3-to 4-fold longer in rats receiving the inhibitory analogues than in the controls. Treatment with antagonist II decrease d the weight of the whole prostate, but neither antagonist changed the weight of testes, anterior pituitary gland, or adrenals. Serum luteinizing hormone, follicle-stimulating hormone, and testosterone levels in Copenhagen F-1 rats bearing Dunning tumors were significantly decreased after treatment with the inhibitory analogues, but progesterone levels were increased. The inhibitory effects of these antagonistic analogues on rat prostate tumors suggest that these compounds might be considered in the development of new types of therapy for prostate carcinoma and other endocrine-dependent neoplasias. (Author abstract) (32 Refs)

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. MORPHOLOGICAL EFFECTS IN PITUITARY TUMOURS FOLLOWING RADIOTHERAPY.

Anniko M, Wersall J
Dept. Otolaryngology, Karolinska Hosp., S-104 01 Stockholm, Sweden
Virchows Arch [Pathol Anat]; 395(1):45-58 1982

Seven cases with different endocrinological types of pituitary tumors were subject to open surgery 6-25 yr after fractionated and 2 mo to 9 yr after single dose irradiation. Two cases had been treated with both types of irradiation. Tumor tissue was analyzed at the light and electron microscopic levels. Hyalinization around blood vessels occurred independent of type of irradiation but required some time to develop. This was not found in one tumor analyzed 2 mo after single dose treatment. Single dose treatment (30-70 Gy) caused extensive fibrosis and few surviving cells in the primary target area. Tumors treated with fractionated dose irradiation (26-45 Gy) showed a large number of tumor cells present 6-8 yr after treatment. Many of these cells revealed morphological damage. The morphological findings of the presently available material

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may indicate that a single dose treatment causes rapid and extensive tumor damage at the site of the primary target but that surviving tumor cells are present outside this area. Fractionated irradiation results in an initial dysfunction with persistance of more or less structurally altered cells for several years. (Author abstract) (24 Refs)

2. CRYOSURGERY OR MICROSURGERY IN THE MANAGEMENT OF ACROMEGALY.

Teasdale GM, Hay ID, Beastall GH, McCruden DC, Thomson JA, Davies DL, Grossart KW, Ratcliffe JG

(c/o Hay) Western General Hosp., Edinburgh EH4 2XU, Scotland

JAMA; 247(9):1289-1291 1982

Fifty-six patients with growth hormone-secreting pituitary adenomas, 28 treated by cryoablation and 28 by microsurgery, have been followed up from 3 to 8 years. Mean serum growth hormone concentrations were less than 10 mU/L in 19 patients (68%) after microsurgery as compared with 7 (25%) after cryosurgery. Hypopituitarism and operative complications were more frequent after cryosurgery. Transsphenoidal microsurgery was particularly successful in reducing growth hormone secretion without impairing normal pituitary function, when the patient had not been previously treated by another method. (Author abstract) (16 Refs)

3. THERAPEUTIC EFFECT ON GALACTORRHEA AND STERILITY IN PROLACTIN-SECRETING PITUITARY ADENOMAS.

Sato O, Tanabe S, Tsuchita H, Nakagawa T, Inoue Y, Daibo M, Uede T, Hotta H

Dept. Neurosurgery, Sapporo Medical Coll., Sapporo 060, Japan

Neurol Med Chir (Tokyo); 21(11):1123-1133 1981

The authors investigated factors responsible for cessation of galactorrhea or restoration of ovulation in 30 women with PRL-secreting pituitary adenomas after surgery with or without bromocriptine. All the patients complained of sterility and 25 patients had galactorrhea. Microsurgical removal of adenomas was performed in all the patients and 15 patients received oral bromocriptine after surgery on account of sustained elevated serum PRL levels. Galactorrhea ceased in 19 out of 25 patients (76.0%) after the treatment. Preoperative serum PRL levels, age of patients at surgery, duration of galactorrhea, history of nursing, severity of galactorrhea and serum estradiol or progesterone levels had no correlation with cessation of galactorrhea. Ovulation was restored in 18 of 30 patients (60.0%) after the treatment and pregnancy was established in 12 patients. The PRL levels where ovulation was restored ranged from there to 57 ng/ml. The normal PRL levels did not inevitably ensure restoration of ovulation. There was no difference in the frequency of restoration of ovulation after the treatment between patients with preoperative PRL levels below 200 ng/ml after surgery. There was a prevalence in the frequency of restoration in amenorrhea Grade I, preoperative duration of sterility of less than 5 yr, microadenomas, a longer postoperative interval normal serum basal LH levels and peak LH levels in response to LH-RH and the presence of positive feedback control to surge LH in response to estrogen. Age of the patients at surgery, elevated dopamine activity in the hypothalamus and serum estradiol or progesterone levels were not correlated with restoration of ovulation. (36 Refs) (In JPN)

4. METERGOLINE IN THE MANAGEMENT OF HYPERPROLACTINEMIC AMENORRHEA AND ANOVULATION.

Falsetti L, Voltolini AM, Crosignani PG, Lotti G, Travaglini P, Faglia G, Cianci A, Palumbo G, Praga C, Pontiroli AE

(c/o Pontiroli) Cattedra di Clinica Medica 8, Ospedale S. Raffaele, 1-20132 Milan, Italy

Gynecol Obstet Invest; 13(2):108-116 1982

Metergoline (MRG: 12 mg/day x 90) was given to 84 women with elevated serum prolactin (PRL) levels. The cause of hyperprolactinemia (HPL) was a pituitary adenoma in 18/84, neuroleptics or oral contraceptives in 7/84, postpartum HPL in 6/64, and unknown in 53/64. The major complaints were amenorrhea in 70/84 and anovulation in 14/84; galactorrhea was present in 50/84. The 90-day course of MRG was completed by 79 patients. Amenorrhea disappeared in 61/65 patients who completed the trial; 59/61 responded within the first 2 mo of treatment. The first menstrual period was followed by other periods in 58/61 patients. Galactorrhea disappeared in 40/50 patients. Ovulation returned in 13/14 evaluable anovulatory patients. All patients were advised to practice nonhormonal contraception, but 14 women became pregnant; 12/14 pregnancies proceeded uneventfully to normal delivery. Serum PRL levels were reduced in 76/79 patients who completed the planned course of MRG. Two of the failures were in patients with pituitary microadenomas, the third had idiopathic amenorrhea. In general, serum PRL levels were reduced to a greater extent in patients who obtained ovulatory cycles than in those who did not; however, some patients achieved ovulatory cycles although their serum PRL levels remained elevated. In 49 patients, the trial was continued for an additional 2 mo, with a reduced MRG dose (8 mg/day; 24/49) or placebo (25/49). Amenorrhea returned within 2 mo in 16/25 placebo-treated and only 5/24 MRG-treated patients. Serum PRL levels increased when amenorrhea recurred. It is concluded that MRG is a safe, effective agent for the treatment of HPL amenorrhea and anovulation. (20 Refs)

5. CHOOSING THE BEST TREATMENT FOR ACROMEGALY.

Christy NP
Brooklyn Veterans Admin. Medical Center, Brooklyn, NY
JAMA; 247(9):1320 1982

Choice of treatment for acromegaly is based on the methods available, individual needs of the patient, and advantages and limitations of each method. Involved is the treatment of endocrine deficiencies, the tumor mass itself, and the consequences of growth hormone hypersecretion. Conventional pituitary radiation and transsphenoidal microsurgery appears to be the most effective, the least damaging, and the most accessible choice. While microsurgery does not damage remaining hormonal functions of the pituitary, cryosurgery does. (5 Refs)

6. ASSOCIATION OF EMPTY SELLA SYNDROME AND PRIMARY HYPERPARATHYROIDISM.

Baker BA, Randall RV, Hodgson SF
Mayo Graduate Sch. Medicine, Rochester, MN
Mayo Clin Proc; 57(4):259-262 1982

This report describes two patients with coexisting primary hyperparathyroidism and the primary empty sella syndrome, and discusses similarities between these two disease entities and the multiple endocrine neoplasia Type 1 syndrome. (Author abstract) (25 Refs)

7. GRANULAR-CELL PITUICYTOMA ASSOCIATED WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 2: CASE REPORT.

Cusick JF, Ho KC, Hagen TC, Kun LE
Dept. Neurosurgery, Medical Coll. Wisconsin, Milwaukee County Medical Complex, 8700 West Wisconsin Ave., Milwaukee, WI, 53226
J Neurosurg; 56(4):594-596 1982

Granular-cell pituicytomas of the neurohypophysis have a controversial histogenesis and oncological behavior. The occurrence of such a tumor in a patient whose father and daughter had endocrine neoplasms suggests a neuroectodermal origin for these tumors. Although all of the conditions considered in this report are unusual clinical entities, their correlation offers considerations in understanding the importance of genetic factors in tumor development. (Author abstract) (18 Refs)

8. SERUM SOMATOMEDIN ACTIVITY IN CHILDREN AFTER SURGERY FOR CRANIOPHARYNGIOMA.

Martinez MJ, Chaussain JL, Schimpff RM, Donnadieu M, Roger M, Job JC
(c/o Chaussain) Laboratoire de Recherches sur la croissance, INSERM U 188, Hopital Saint-Vincent-de-Paul, 74, avenue Denfert-Rochereau, 75014 Paris France
Arch Fr Pediatr; 38(Supplement1):881-886 1981

Somatomedin (ST) activity and blood hormone levels were studied in 22 children (10 males, 12 females; 5-15 yr old) who had undergone surgery for craniopharyngiomas. The patients exhibited varying rates of growth. Serum growth hormone levels were consistently less than 1 nanog/ml. The correlation between serum ST activity and the speed of growth showed a highly significant correlation. No correlation was observed between serum ST activity and other clinical parameters: percentage of excess wt and recent variations in wt. No correlation was found between ST activity and blood concentrations of insulin and prolactin. A negative correlation between ST activity and plasma cortisol levels was observed when only patients not receiving hydrocortisone therapy were considered; among these patients, a negative correlation was also found in comparing serum cortisol and growth rate. When the total group of patients was considered no such negative correlations were noted. Patients receiving thyroid hormones showed a positive correlation between ST activity serum concentrations of triiodothyronine and thyroxine. Triiodothyronine levels were positively correlated with the rate of growth. The results indicated that in children operated on for craniopharyngioma, growth is related to a generation of ST independent of growth hormone secretion and is closely controlled by endogenous secretions of cortisol and thyroid hormones. (15 Refs) (In FRE)

THYROID TUMORS

9. NEEDLE BIOPSY IN THE ASSESSMENT AND MANAGEMENT OF HYPOFUNCTIONING THYROID NODULES.

Goldfarb WB, Bigos TS, Eastman RC, Johnston H, Nishyama RH
Dept. Surgery, Maine Medical Center, Portland, ME, 04102
Am J Surg; 143(4):409-412 1982

Needle biopsy of hypofunctioning solitary thyroid nodules provides direct diagnostic information which would be otherwise obtainable only by surgery. The technique is safe and cost-effective. It provides a high diagnostic yield. It is also useful in planning surgery and reducing dependence on frozen-section diagnosis, which is often difficult with thyroid nodules. Technical and interpretative precautions are discussed. Of 192 patients undergoing this procedure, a satisfactory specimen was obtained in 95%. Needle aspiration biopsy (fine needle) was done in 110 patients with good cytologic correlation. Of 52 glands subsequently excised, carcinoma was present in 22 (42%). The preoperative diagnosis had been made in 19 (86%) of the latter group. This procedure is recommended for consideration in the assessment and management of hypofunctioning thyroid nodules. (Author abstract) (17 Refs)

10. AGE-ASSOCIATED C-CELL HYPERPLASIA IN THE HUMAN THYROID.

Gibson WG, Peng TC, Croker BP
(c/o Croker) Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Am J Pathol; 106(3):388-393 1982

C cells in 26 normal human thyroids from forensic autopsies were identified by immunoperoxidase staining for calcitonin. C-cell concentrations and total C-cell numbers were determined with the use of morphometric techniques. There was great variation in C-cell density within a given gland and among individuals, although C cells tended to concentrate about one third of the way down the vertical axis of the lateral lobes. Densities of 1-2,000 cells/cu mm were found in the third and later decades. In addition there was a statistically significant (p less than 0.01) positive Spearman correlation between total C-cell numbers and age in males. C-cell hyperplasia appears to be an age-related phenomenon that may have physiologic significance and must be taken into consideration in evaluation of thyroid glands for the diagnosis of premalignant lesions of C cells. (Author abstract) (20 Refs)

11. SOLID THYROID NODULES.

Perry HA
Dept. Surgery, East End Memorial Hosp., Birmingham, AL, 35206
Am Surg; 48(4):170-174 1982

The management of solitary thyroid nodules remains controversial. A series of 120 patients having operations for a solitary thyroid nodule is retrospectively reviewed. Neoplasia rate was found to be 29.1% and the malignancy rate, 11.7%. These are compared with other studies emphasizing the use of thyroid imaging with radioactive substances or ultrasonography and invasive techniques such as fine needle aspiration where the yields of neoplasia and malignancy are, respectively, 18-65% and 8-29%. Current techniques allow identification of solitary nonfunctioning and solid nodules, and operation for these should increase the yield of cancer while reserving thyroid suppression and possibly fine needle aspiration for the management of other lesions. (Author abstract) (14 Refs)

12. PRIMARY HYPERPARATHYROIDISM AND NONMEDULLARY THYROID CANCER.

Linos DA, Van Heerden JA, Edis AJ
(c/o van Heerden) Dept. Surgery, Mayo Clinic, Rochester, MN, 55905
Am J Surg; 143(3):301-303 1982

Of 2,058 patients who had surgically proven primary hyperparathyroidism at the Mayo Clinic from 1965 through 1979, 51 or 2.5% had associated nonmedullary thyroid carcinoma. A history of radiation exposure to the head and neck was obtained in 14 of 43 patients questioned. Thyroid disease consisted of Grade 1 papillary adenocarcinoma in 48 cases and pure follicular adenocarcinoma in three cases. The parathyroid disease included 41 single adenomas and 5 cases of parathyroid hyperplasia; 5 patients had 2 adenomas. At follow-up, none of the patients had evidence of metastatic thyroid carcinoma. Ten patients were receiving calcium or vitamin D supplementation for protracted hypocalcemia presumably due to the increased insult to the parathyroids from combined bilateral thyroidectomy and parathyroidectomy. More conservative thyroidectomy, along with parathyroid autotransplantation when indicated, will provide definitive treatment of the thyroid cancer and at the same time minimize the risk of postoperative hypoparathyroidism. (Author abstract) (27 Refs)

13. T3 TOXICOSIS DUE TO NONMETASTATIC FOLLICULAR CARCINOMA OF THE THYROID.

Pont A, Spratt D, Shinn JB
Dept. Medicine, Children's Hosp. San Francisco, P.O. Box 3805, San Francisco, CA, 94119
West J Med; 136(3):255-258 1982

Hyperthyroidism due to nonmetastatic carcinoma of the thyroid in a 52 yr old woman is reported. Clinical findings included an enlarged thyroid gland, normal thyroxine, and elevated triiodothyronine level. Thyroid stimulating hormone was undetectable. Histological examination following partial thyroid resection revealed follicular cell carcinoma. Metastases were not suspected due to I131 uptake restricted to the thyroid region. Thyroid carcinoma is apparently more common in regions termed 'goiter belts.' (25 Refs)

14. GASTRIN RESPONSES TO A TEST MEAL IN PATIENTS WITH FAMILIAL MEDULLARY THYROID CARCINOMA.

O'Dorisio TM, Falko JM, Cataland S, Almoney RW, George JM, Mazzaferri EL, Reynolds JC
Div. Endocrinology, Ohio State Univ. Hosp., 410 West 10th Ave., Columbus, OH, 43210
J Clin Endocrinol Metab; 54(4):798-802 1982

The serum gastrin response to a standard test meal was evaluated in patients with familial medullary thyroid carcinoma (MTC) and in normal subjects. Patients with MTC and elevated plasma calcitonin levels had a lower gastrin response to the test meal than did normal persons or MTC patients who had normal calcitonin levels postthyroidectomy. There was no significant difference between the mean gastrin response of the normal group and that of the MTC patients with normal calcitonin levels. The serum gastrin response was studied before and after thyroidectomy in four patients. In all four, the postoperative response was greater than the preoperative one. We conclude that patients with MTC may have reduced gastrin responses to a test meal. This effect may be related to circulating calcitonin, somatostatin, or other factors related to familial MTC. (Author abstract) (18 Refs)

15. PLASMA SOMATOSTATIN IN NORMAL SUBJECTS AND IN VARIOUS DISEASES: INCREASED LEVELS IN SOMATOSTATIN-PRODUCING TUMORS.

Saito H, Saito S
Dept. Lab. Medicine, Sch. Medicine, Univ. Tokushima, 2-50 Kuramoto-Cho, Tokushima 770, Japan
Horm Metab Res; 14(2):71-76 1982

The plasma levels of somatostatin (SRIF) were studied in normal subjects and patients with various disorders by a sensitive and specific radioimmunoassay. In 45 normal subjects, the fasting plasma SRIF concentrations were 13.3 +-5.3 pg/ml (mean +- SD). Very high concentrations of plasma SRIF, ranging from 125.0 pg/ml to 400.0 pg/ml, were found in all four patients with medullary carcinoma of the thyroid examined and the SRIF levels were changed in parallel with their clinical course after resection of the tumor. A case of pheochromocytoma also showed a relatively high SRIF concentration in plasma (47.0 pg/ml), but the plasma SRIF level decreased to 8.7 pg/ml after removal of the tumor. In normal subjects, plasma SRIF levels did not fluctuate during 2 hr-observation period in basal state. Glucagon (1 mg, iv) and secretin (3 CHRU/kg BW, iv infusion over 30 min) had no effect on the SRIF levels in the peripheral blood plasma of normal subjects. On intravenous infusion of arginine (0.5 g/kg BW) over 30 min, all six normal subjects showed a significant increase in plasma SRIF 30-45 min after the start of the infusion (basal value, 11.6 +-1.5 pg/ml; peak value, 27.2 +-3.0 pg/ml; p less than 0.005). Two cases of medullary thyroid carcinoma showed exaggerated responses after the arginine administration (increases of 103 pg/ml and 157 pg/ml, respectively), suggesting that SRIF was released from the tumor. These findings indicate that plasma SRIF determination in the basal state and after arginine administration is useful for detecting and following up SRIF-producing tumors. (Author abstract) (32 Refs)

16. SERUM THYROGLOBULIN IN THE MANAGEMENT OF PATIENTS WITH THYROID CANCER.

Barsano CP, Skosey C, DeGroot LJ, Refetoff S
(c/o DeGroot) Thyroid Study Unit, Univ. Chicago, Box 138, 950 E 59th St., Chicago, IL, 60637
Arch Intern Med; 142(4):763-767 1982

We have reviewed our experience with the management of patients with thyroid cancer to assess the potential benefits of employing the serum thyroglobulin assay in patient management programs and to determine the optimal conditions for this application. Serum thyroglobulin levels were found to be more reliable when obtained from hypothyroid patients. Levels of thyroglobulin greater than 10 ng/mL appeared to be abnormally elevated in both thyroidectomized patients prior to radioactive iodine therapy (Group 1) and in thyroidectomized patients after radioactive iodine therapy (Group 2). Elevated thyroglobulin levels were found to be useful indicators of the presence of metastatic disease, whereas normal thyroglobulin levels were reliable indicators of the absence of metastases. In Group 1 patients, elevated thyroglobulin levels reliably predicted the presence of important total body scan uptake. In Group 2 patients, normal thyroglobulin levels reliably predicted the absence of total body scan uptake. The serum thyroglobulin assay can substantially reduce the need for repetitive total body scanning in the follow-up of Group 2 patients with thyroid cancer. (Author abstract) (22 Refs)

PARATHYROID TUMORS

17. RADIOIMMUNOASSAY FOR THE MIDDLE REGION OF HUMAN PARATHYROID HORMONE USING AN HOMOLOGOUS ANTISERUM WITH A CARBOXY-TERMINAL FRAGMENT OF BOVINE PARATHYROID HORMONE AS RADIOLIGAND.

Mallette LE, Tuma SN, Berger RE, Kirkland JL
c/o Dr. L. E. Mallette, Medical Service (111E), Veterans Admin. Medical Center, 2002 Holcombe Blvd., Houston, TX, 77211
J Clin Endocrinol Metab; 54(5):1017-1024 1982

A new type of RIA for human parathyroid hormone (hPTH) is described. The antiserum was generated in a goat against hPTH, and the radioligand is a carboxy-terminal fragment of bovine PTH (bPTH). Although the antiserum is bivalent, use of the fragment as tracer yields an assay monospecific for the midregion of the PTH molecule. The assay can detect 0.3 fmol/tube of intact hPTH-(1-84) or 0.1 fmol synthetic hPTH-(44-68), but does not detect hPTH-(1-34), hPTH-(53-84), or bPTH-(28-48). Immunoreactive PTH (iPTH) was detectable in 85 of 92 normal subjects, with a normal range of about 0.1-0.5 microU/ml hPTH Research Standard 75/549. iPTH was undetectable in 22 consecutive severely hypoparathyroid patients and was above normal in 147 of 158 patients with primary hyperparathyroidism. In 60 patients with nonparathyroid hypercalcemia, iPTH averaged 20% lower than in normal subjects, but was still detectable in 80%. Mean iPTH values in hypercalcemia due to malignancy or other nonparathyroid causes were indistinguishable. When renal insufficiency supervened in those with nonparathyroid hypercalcemia, iPTH tended to increase, and reached levels three- to four-fold above normal when serum creatinine was above 5 mg/dl. In chronic renal failure, iPTH levels were 5-to 36-fold above normal in patients just beginning hemodialysis and 60-to 600-fold evaluated in those with severe osteitis fibrosa. The distribution of iPTH values in hypercalcemic chronic hemodialysis patients was bimodal; values were about 600-fold elevated in patients whose hypercalcemia responded to parathyroidectomy (tertiary hyperparathyroidism), but only 2-to 20-fold increased in those with nonparathyroid hypercalcemias. The assay was sensitive enough to detect changes that occurred spontaneously in normal subjects or were induced by EDTA infusion. The assay was also useful in detecting venous of PTH. This new assay, with its excellent sensitivity, provides a useful diagnostic and research tool for studies of human parathyroid function. (Author abstract) (33 Refs)

ADRENAL TUMORS

18. COMPUTED TOMOGRAPHY VERSUS ULTRASOUND OF THE ADRENAL GLAND: A PROSPECTIVE STUDY.

Abrams HL, Siegelman SS, Adams DF, Sanders R, Finberg HJ, Hessel SJ, McNeil BJ
Dept. Radiology, Harvard Medical Sch., 25 Shattuck St., Boston, MA, 02115
Radiology; 143(1):121-128 1982

A prospective study of the accuracy of computed tomography (CT) and ultrasound was undertaken in 112 consecutive patients with suspected adrenal disease. CT had a sensitivity of 84% (47/56), a specificity of 98% (55/56), and an accuracy of 90%. Ultrasound had a sensitivity of 79% (22/28), a specificity of 61% (14/23), and an overall accuracy of 70%. When patients with Cushing disease and adrenal hyperplasia were excluded, and only masses such as pheochromocytoma, adenoma, and carcinoma were considered, the sensitivity of both CT and ultrasound was increased. Receiver operating characteristic (ROC) curves differed for CT and ultrasound, and strongly supported the diagnostic superiority of CT. (Author abstract) (34 Refs)

19. ADRENAL PSEUDOTUMORS ON COMPUTED TOMOGRAPHY.

Berliner L, Bosniak MA, Megibow A
(c/o Bosniak) Dept. Radiology, New York Univ. Medical Center, Univ. Hosp., 560 First Ave., New York, NY, 10016
J Comput Assist Tomogr; 6(2):281-285 1982

Masses arising in the adrenal gland may be simulated on computed tomography (CT) by a number of anatomical structures and variations, and by certain pathological conditions in adjacent organs. These adrenal pseudotumors include the following: fluid-filled gastric fundus, prominent splenic lobulations, upper pole renal masses, tortuous splenic vessels, and pancreatic masses. These conditions, which represent pitfalls in the diagnosis of adrenal tumors on CT, are demonstrated and discussed. Certain guidelines will be discussed so that these potential pitfalls may be avoided. (Author abstract) (9 Refs)

20. ADRENAL GLAND IDENTIFICATION: PREOPERATIVE ASSESSMENT.

Kalff V, Sisson JC, Beierwaltes WH
(c/o Sisson) Div. Nuclear Medicine, Univ. Michigan, Medical Center, Ann Arbor, MI, 48109
Surgery; 91(4):374-376 1982

The perioperative management of patients with pheochromocytoma may be complicated by the tumor's location in a single remaining adrenal gland. This case report illustrates the complementary use of adrenocortical and medullary scintigraphy in the assessment of a patient who presented this potential problem. (Author abstract) (10 Refs)

21. PHEOCHROMOCYTOMA: CURRENT STATUS AND CHANGING TRENDS.

van Heerden JA, Sheps SG, Hamberger B, Sheedy PF, Poston JG, ReMine WH
Mayo Clinic, Rochester, MN, 55905
Surgery; 91(4):367-373 1982

From 1971 through 1980, 106 patients underwent operations for pheochromocytoma. Twelve patients had a pheochromocytoma as a manifestation of the multiple endocrine neoplasia Type 2 syndrome. Twenty patients were found to have extra-adrenal paragangliomas. Fifteen patients (14%) had malignant tumors; eight of these tumors were encountered in the group with extra-adrenal lesions. The cumulative survival probability at 5 yr was 53%. Determination of urinary metanephrines and vanillylmandelic acid were the most sensitive diagnostic aids, with accuracy rates of 95% and 89%, respectively. In recent years, the measurement of fractionated urinary and plasma catecholamine levels has greatly increased the diagnostic accuracy. Preoperative localization of pheochromocytoma has improved during the last decade. Nephrotomography, selective angiography, and venous sampling have essentially been abandoned in favor of computed tomography. With an accuracy of more than 90%, computed tomography represents the major step forward in the overall management of pheochromocytoma during the past decade. (Author abstract) (15 Refs)

22. CONVERTING ENZYME INHIBITION WITH CAPTOPRIL IN PATIENTS WITH PRIMARY HYPERALDOSTERONISM.

Luderer JR, Demers LM, Harrison TS, Hayes AH

Div. Clinical Pharamcology, Milton S. Hershey Medical Center, Hershey, PA, 17033

Clin Pharmacol Ther; 31(3):305-311 1982

The humoral and hemodynamic effects of converting enzyme inhibition with captopril are presented in two patients with primary hyperaldosteronism (PHA). In all, 20 patients with resistant hypertension were treated with the angiotensin converting enzyme inhibitor captopril. In 18 patients with essential or renovascular hypertension mean (+-SEM) plasma renin activity (PRA) rose from 5.0 +-1.4 to 35.3 +-5.3 ng/ml/hr (p less than 0.001) and mean (+- SEM) plasma aldosterone (PA) declined from 25.8 +-2.9 to 15.1 +-1.9 ng/ml (p less than 0.01) after captopril. In two patients with PHA the PRA was not stimulated by converting enzyme inhibition, although there was modest decline in PA and a temporary reduction in blood pressure. After surgical removal of aldosterone-producing adenomas, PRA responded appropriately to captopril. These cases illustrate that a disease process can modify the response to a drug and demonstrate that, in patients with PHA, captopril does not stimulate PRA, induces only minor decrements in PA, and is relatively ineffective as an antihypertensive. (Author abstract) (12 Refs)

23. ADRENAL HEMANGIOMA.

Lee WJ, Weinreb J, Kumari S, Phillips G, Pochaczevsky R, Pillari G

Dept. Radiology, Long Island Jewish Hillside Medical Center, New Hyde Park, NY, 11042

J Comput Assist Tomogr; 6(2):392-394 1982

A case of adrenal cavernous hemangioma is described, and the literature is reviewed. It is the first reported case of adrenal hemangioma that has been documented by ultrasound and computed tomography. Although rare, a hemangioma should be considered in the differential diagnosis of a calcified adrenal mass. (Author abstract) (7 Refs)

24. MASSIVE HYPERPLASIA OF TESTICULAR ADRENAL RESTS IN A PATIENT WITH NELSON'S SYNDROME.

Johnson RE, Scheithauer B

Section Publications, Mayo Clinic, Rochester, MN, 55905

Am J Clin Pathol; 77(4):501-507 1982

The case of a 23-yr-old man with Nelson's syndrome is presented. He had undergone bilateral adrenalectomy at age 15 yr for Cushing's syndrome. Postoperatively, his cushingoid features resolved; however, 13 mo later, he became hyperpigmented and showed radiographic evidence of sellar enlargement and midline expansion of the sellar floor. In 1972, he received radiation therapy to the pituitary gland. He underwent transsphenoidal hypophysectomy in 1974 and 1975 for recurrent pituitary adenoma, and recurrent Cushing's syndrome developed concomitantly with bilateral firm testicular masses in 1978. External scanning with NP-59 localized steroid production to the testes, and bilateral orchiectomy was performed. Immunohistochemical studies of the pituitary tumor confirmed the presence of adrenocorticotropic hormone, and morphologic and ultrastructural examinations of the testes supported the adrenal nature of the testicular tumors. (Author abstract) (8 Refs)

25. EVALUATION OF THE 6-HOUR INTEGRATED CONCENTRATION OF CORTISOL AS A DIAGNOSTIC PROCEDURE FOR CUSHING'S SYNDROME.

Zadik Z, De Lacerda L, Kowarski AA

(c/o Kowarski), Univ. Maryland Sch. Medicine, Howard Hall Tower 10-047, Baltimore, MD, 21201

J Clin Endocrinol Metab; 54(5):1072-1074 1982

The diagnostic value of the 24-hr integrated concentration (IC) test of cortisol (IC-24-F) was found to be superior to the value of both urinary 17OHCS and urinary free cortisol tests. The IC-24-F test is too cumbersome for widespread clinical use. The purpose of the present study was to evaluate the diagnostic value of an abbreviated and practical 6-hr IC of cortisol (IC-6-F) test. The IC of cortisol (IC-F) was measured in 68 normal subjects and 13 patients with surgically proven Cushing's syndrome. A portable nonthrombogenic constant blood withdrawal system was used over a 24-hr period. The IC-F was measured in plasma withdrawn during each 0.5 hr period (IC-1/2-F). The mean of 12 consecutive measurements of IC-1/2-F yielded the IC-6-F. The mean of all the IC-1/2-F collected over a 24-hr period constituted the IC-24-F. The IC-1/2-F of the patients and their IC-6-F from 0800-1400 hr, 1400-2000 hr, and 2000-0200 hr overlapped the corresponding levels in the control subjects. There was no overlap between the IC-24-F and the IC-6-F (from 2000-0200 hr) of the patients and the control subjects. It was concluded that the diagnostic value of a 6-hr IC-F test conducted during the afternoon and early part of the night is equal to the diagnostic value of the 24-hr IC-F test. (Author abstract) (13 Refs)

26. INCREASED PLATELET CATECHOLAMINE CONTENT IN PHEOCHROMOCYTOMA: A DIAGNOSTIC TEST IN PATIENTS WITH ELEVATED PLASMA CATECHOLAMINES.

Zweifler AJ, Julius S

Div. Hypertension, Univ. Michigan Medical Center, Box 48, R 6669 Kresge Medical Res. Building, Ann Arbor, MI, 48109

N Engl J Med; 306(15):890-894 1982

Measurement of platelet catecholamine content in 16 patients (5 male, 11 female; 1-62 yr old) with suspected pheochromocytoma and elevated plasma catecholamine levels [norepinephrine greater than 650 picog (pg)/ml, epinephrine greater than 120 pg/ml] is reported. Catecholamine content was determined by radioenzymatic assay. Of the subjects, 10 with documented pheochromocytoma had significantly increased platelet catecholamine content. The remaining six patients had normal platelet catecholamine levels and no tumor. Following tumor removal, platelet catecholamines tended to return to normal more slowly than plasma catecholamines. Patients suspected of having pheochromocytoma on clinical grounds and who have plasma norepinephrine levels greater than 2000 pg/ml should be sent directly for localizing procedures. In patients suspected of pheochromocytoma and whose plasma norepinephrine concentration is elevated but less than 2000 pg/ml, determination of platelet catecholamine content may be a useful intermediate step in diagnosis. (17 Refs)

27. METHIONINE-ENKEPHALIN AND LEUCINE-ENKEPHALIN IN HUMAN SYMPATHOADRENAL SYSTEM AND PHEOCHROMOCYTOMA.

Yoshimasa T, Nakao K, Ohtsuki H, Li S, Imura H
Second Div., Dept. Medicine, Kyoto Univ. Sch. Medicine, Kyoto 606, Japan
J Clin Invest; 69(3):643-650 1982

To elucidate the physiological and pathophysiological significance of methionine- and leucine-enkephalin (Met- and Leu-enkephalin, respectively) in human sympathoadrenal system, the contents of these peptides in normal human sympathetic nervous system, adrenal medulla, and pheochromocytomas were determined by specific radioimmunoassays combined with reverse-phase high-performance liquid chromatography. Met-enkephalin-like and Leuenkephalin-like immunoreactivity (Met-enkephalin-LI and Leu-enkephalin-Li, respectively) were detected by radioimmunoassay in adrenal glands, adrenal medulla, stellate ganglia, sympathetic trunks, and celiac ganglia, and their contents in adrenal medulla were highest. Existence of authentic Met- and Leu-enkephalin was confirmed by reverse-phase high-performance liquid chromatography. Met-enkephalin was approx 74% of Met-enkephalin-LI, whereas Leu-enkephalin was approx 30% of Leu-enkephalin-LI in human adrenal medulla. The ratio of Met- to Leu-enkephalin was 2.6 in human adrenal medulla, whereas it was higher in sympathetic ganglia or trunks. In four cases of pheochromocytoma marked difference in Met- and Leu-enkephalin contents was found between medullary and extramedullary tumors. The contents were about three orders higher and the Met- to Leu-enkephalin ratio was lower in medullary than in extramedullary pheochromocytomas, reflecting the tissues where the tumors arose. These results suggest the physiological roles of Met- and Leu-enkephalin in sympathetic nervous systems and adrenal glands and their pathophysiological significances in pheochromocytomas. (Author abstract) (21 Refs)

PANCREAS TUMORS

28. PANCREATIC ENDOCRINE TUMORS: IMMUNOCYTOCHEMICAL ANALYSIS OF 125 TUMORS.

Heitz PU, Kasper M, Polak JM, Kloppel G
Dept. Pathology, Univ. Basel, Schonbeinstrasse 40, CH-4056 Basel, Switzerland
Hum Pathol; 13(3):263-271 1982

One hundred twenty-five pancreatic endocrine tumors were analyzed by immunocytochemistry using various antisera. Twenty-three of 27 insulinomas, 10 of 10 PP-omas (PP: pancreatic polypeptide) and 15 of 30 'nonsecreting' tumors were benign, whereas 8 of 13 glucagonomas, 16 of 24 gastrinomas, and 16 of 21 VIP-omas (VIP: vasoactive intestinal polypeptide) were malignant. As a rule, the hormone secreted by the tumor and causing clinical symptoms could be localized by immunocytochemistry. Fifty of 95 active tumors were found to contain cells immunoreactive to peptide(s) not causing clinical symptoms, and 15 of 30 'nonsecreting' tumors were shown to be multicellular. By electron microscopy more than one cell type could be identified in 12 tumors. Histologically, the growth pattern of the tumors was very variable and distribution of immunoreactive cells was distinctly patchy. Radioimmunoassay on extracts of 20 of 27 tumors confirmed the presence of peptides visualized by immunocytochemistry. In 17 of 22 specimens, groups of endocrine cells in close contact with ductules were found in the pancreatic parenchyma distant from the tumor. Pancreatic endocrine tumors probably arise from the pancreatic ductular epithelium. They are often multicellular, producing and sometimes secreting more than one hormone or hormone-like substance. They represent highly complex biologic systems in which the interrelationship of various gastrointestinal-pancreatic hormones can be studied. (Author abstract) (45 Refs)

GONADAL TUMORS

29. POLYEMBRYOMA OF OVARY PRODUCING ALPHA-FETOPROTEIN AND HCG: IMMUNOPEROXIDASE AND ELECTRON MICROSCOPIC STUDY.

Takeda A, Ishizuka T, Goto T, Goto S, Ohta M, Tomoda Y, Hoshino M

Lab. Ultrastructure Res., Aichi Cancer Center Res. Inst., Chikusaku, Nagoya 464, Japan

Cancer; 49(9):1878-1889 1982

Polyembryoma of ovary producing alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) was studied by indirect immunoperoxidase method for AFP and HCG, and electron microscopy. Clinically, this patient showed pseudoprecocious puberty caused by elevated HCG which is synthesized by trophoblastic cells in polyembryoma. She is put under VAC (vincristine, actinomycin-D, cyclophosphamide) chemotherapy after operation and shows no signs of recurrence including reelevation of serum AFP at 5 mo after operation. Embryoid bodies which we studied correspond to normal embryo at 15- or 16-day stage. Immunoperoxidase study showed that AFP is synthesized by yolk sac cells of the embryoid bodies and HCG is synthesized by syncytiotrophoblastic cells. The finding about AFP synthesis suggests that normal embryo at 15-or 16-day stage may begin AFP synthesis. Electron microscopic study showed that each part of the embryoid bodies had some characteristic structures. Most striking features found in the cytodifferentiation of the embryoid bodies were noticed in some special differentiation of plasma membrane and existence of surface coat. Desmosomes were found in endodermal cells and yolk sac cells. Ectodermal cells were attached to each other by zonulae occludentes and adherentes. Microvilli were found in ectodermal cells and yolk sac cells. Two different kinds of surface coat were found in mesodermal cells and lining cells of yolk sac cavity: thin-layered deposit of electron-dense material covering the plasma membrane facing intercellular space of mesodermal cells and endodermal cells, and thick-layered deposit of electron-dense material which covered the plasma membrane facing yolk sac cavity of endodermal cells and yolk sac cells. Presence of similar characteristic material in RER of yolk sac cells led us to speculate that thick deposit was synthesized by yolk sac cells and secreted into yolk sac cavity. Combined with immunoperoxidase study by light microscopy, we assume that this thick-layered deposit has some close relation to AFP. (Author abstract) (23 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

30. CELLULAR LOCALIZATION OF ESTROGEN BINDING SITES IN HUMAN BREAST CANCER.

Hanna W, Ryder DE, Mobbs BG

Dept. Lab., Women's Coll. Hosp., 76 Greenville St., Toronto, Ontario M5S 1B2, Canada

Am J Clin Pathol; 77(4):391-395 1982

Biopsy specimens from 52 consecutive cases of primary human breast cancer were collected over a period of 7 mo and included in a study for histochemical localization of estrogen binding sites (EBS), using a fluorescein labeled Estradiol conjugate. Cryostat frozen sections from each tumor were examined to determine the localization of the tracer and to evaluate the percentage of positive cells in a given tumor. Results are correlated with the values of the biochemical assay for the estrogen receptor (ER) protein done on the same tumor. The localization of EBS by a tracer is a simple technique that can be done and interpreted in any surgical pathology laboratory. It was concluded that this method could be a valuable supplementary technique to the biochemical assay; allowing more accurate selection of patients and prediction of their response to endocrine therapy. Clinical follow-ups are extremely necessary to evaluate the suitability and the accuracy of the technique in choosing breast cancer patients for endocrine manipulation. (Author abstract) (17 Refs)

31. EFFECTS OF ENDOCRINE THERAPY ON STEROID-RECEPTOR CONTENT OF BREAST CANCER.

Taylor RE, Powles TJ, Humphreys J, Bettelheim R, Dowsett M, Casey AJ, Neville AM, Coombes RC

(c/o Coombes) Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England

Br J Cancer; 45(1):80-85 1982

In order to determine the mechanisms of relapse following response to endocrine therapy, we have measured the estrogen receptor (RE) content of biopsies of breast cancer in patients receiving various types of endocrine treatment. RE content fell in responding (means of 260.2 to 12 fmol/mg protein) and in nonresponding (means of 155.1 to 31.8 fmol/mg protein) patients who had measurable receptor at the start of treatment. Some of these patients, and a further group of responders to endocrine therapy, were monitored until relapse. Tumor biopsies at the time of relapse showed that 10/14 tumor samples contained significant RE (mean of 86.7 fmol/mg protein; range less than 10-271 fmol/mg protein) after successful endocrine therapy. No relationship could be found between RE content and plasma gonadotrophin or steroid-hormone concentration, but the fall in RE content correlated with reduced numbers of tumor cells in the biopsy. These results indicate that relapse following successful endocrine therapy in breast cancer does not appear to be due to the emergence of RE-negative tumor cells. The fall in RE content during response to endocrine therapy may be due to reduced tumor-cell content of the biopsy. (Author abstract) (19 Refs)

32. ADJUVANT TAMOXIFEN THERAPY FOR EARLY BREAST CANCER: AN EXPERIMENTAL STUDY WITH REFERENCE TO OESTROGEN AND PROGESTERONE RECEPTORS.

Wilson AJ, Tehrani F, Baum M

Dept. Surgery, King's Coll. Hosp. Medical Sch., Denmark Hill, London SE5 8RX, England

Br J Surg; 69(3):121-125 1982

There is very little known about the subsequent behavior of breast cancer following adjuvant endocrine therapy or the effect of this therapy on the estrogen and progesterone receptor content of recurrent disease. Mammary tumors were induced in Sprague-Dawley rats using N-nitrosomethylurea. In two experiments animals were treated with tamoxifen at different doses prior to the appearance of tumors. Tamoxifen prolonged the induction time and reduced the total number of tumors. Subsequent treatment of established tumors exposed to tamoxifen in the induction period demonstrated a reduced response to further tamoxifen therapy. There was no difference in the estrogen receptor content of the tumors previously exposed to tamoxifen, but there was a significant reduction in the progesterone receptor content. The results suggest that: (a) patients treated with adjuvant tamoxifen therapy will show a delay in the appearance of recurrent disease with a reduced response to further tamoxifen therapy; (b) the model may provide an in vivo method to examine the relationships between estrogen and progesterone receptors and response to endocrine therapy. (Author abstract) (34 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

33. EFFECT OF CYTOTOXIC THERAPY ON SEXUALITY AND GONADAL FUNCTION.

Chapman RM

Walter Reed Army Inst. Res., Washington, DC, 20012

Semin Oncol; 9(1):84-94 1982

The effects of cytotoxic therapy on physiology, reproduction, gonadal dysfunction, sexual and emotional factors, and ageing are discussed. Severity of gonadal dysfunction depends upon total drug dose and patient age at the time of therapy. Generally, cytotoxic agents produce premature gonadal dysfunction in men and premature gonadal failure in women. Men develop azoospermia and compensated Leydig-cell function; women sustain ovarian damage causing impaired fertility in the short term and early ovarian failure later. Oncologists are often unaware of sexual problems of patients, who tend to discuss the problems with their families but not their doctors. Diagnosis can often be accomplished with a questionnaire followed by such procedures as sperm count and hormone level measurements. Treatment involves counseling and often hormone replacement therapy. Prognosis should be considered when counseling young patients on parenthood. (93 Refs)

34. ASSESSMENT OF THE LONG-TERM EFFECTS OF PRIMARY RADIATION THERAPY FOR BRAIN TUMORS IN CHILDREN.

Danoff BF, Cowchock S, Marquette C, Mulgrew L, Kramer S
Dept. Radiation Therapy and Nuclear Medicine, Hosp. Univ. Pennsylvania, Philadelphia, PA, 19104
Cancer; 49(8):1580-1586 1982

One-hundred-twelve children with primary brain tumors received definitive radiotherapy between the yr 1958-1979. Sixty-nine patients were alive at intervals of 1-21 yr. Thirty-eight patients underwent neurologic and endocrine evaluation, psychologic and intelligence testing, and assessment for second malignancy post-treatment. A second intracranial malignancy developed in one child, for an incidence of 1.6%. Performance status was good to excellent in 89% of the patients studied. Seventeen percent of the group were mentally retarded. Behavioral disorders were identified in 39% of the patients, 59% of the mothers, and 43% of the fathers. Of the 23 patients with nonparasellar tumors, 6 were found to have growth hormone deficiency, including 2 patients with panhypopituitarism. Disability was related to age under 3 yr at the time of treatment and tumor extension to the hypothalamus. (Author abstract) (33 Refs)

35. PARANEOPLASTIC ENDOCRINOPATHIES ASSOCIATED WITH NONRENAL GENITOURINARY TUMORS.

Altaffer LF
Dept. Urology, Naval Regional Medical Center, Camp Lejeune, NC
J Urol; 127(3):411-416 1982

The ectopic or inappropriate production of parathyroid hormone (PTH), catecholamines (CTA), serotonin (ST), human chorionic gonadotropin (HCGT), adrenocorticotropic hormone (ACTH), antidiuretic hormone (ADH), calcitonin, estrogens (ES), human placental factor (HPF), erythropoietin, insulin-like substances, and prostaglandins associated with various renal tumors is reviewed. Several case reports of apparent PTH secretion by urothelial tumors exist. In all of the cases resolution of the hypercalcemia followed definite treatment of the cancer. Diagnosis of pheochromocytoma is made by measuring elevated serum, urinary CTA and metabolites. Prognosis is generally good but long-term follow-up with urinary levels of CTA or the metabolites is recommended. Signs and symptoms of some carcinoid tumors are probably caused by excessive production of ST. The secretion of HCGT by testicular neoplasms is well known and the use of HCGT as a tumor marker is applied in practice. ACTH was identified in three cases of carcinoma of the prostate. In 1969, a case of carcinoma of the prostate with evidence of ectopic secretion of ADH by the neoplasm was reported. The secretion of a thyroid stimulating hormone-like substance has been reported in association with trophoblastic tumors in women and in two cases of testis tumors. The secretion of ES, androgens, pregnanediol, and luteinizing hormone, has been associated with Leydig cell tumors, gonadal stromal tumors, and gonadoblastomas. The identification of HPF in the syncytiotrophoblastic cells in malignant teratoma of the testis was reported in 1966. Hypoglycemia has been shown to be associated with a variety of extrapancreatic tumors. Hormonally active tumors frequently demonstrate undifferentiated or anaplastic histologic patterns and, in general, patients with hormonally active tumors appear to have a poor prognosis. (83 Refs)

36. RESECTION OF GASTRINOMA IN THE ZOLLINGER-ELLISON SYNDROME.

Barreras RF, Mack E, Goodfriend T, Damm M
CSC H6/518, 600 Highland Ave., Madison, WI, 53792
Gastroenterology; 82(5,part1):953-956 1982

Patients with the Zollinger-Ellison syndrome have been managed by total gastrectomy and more recently, by the use of H2-receptor antagonists. An alternative approach has been to identify those who might be cured by excision of a pancreatic islet-cell tumor without removal of the stomach. The course of such a patient is reported. A 40-yr-old man with massive gastric hypersecretion, acid-peptic disease, diarrhea, and elevated serum gastrin was treated by excising a pancreatic gastrinoma. Serum gastrin and gastric secretion became and have remained normal for 7 yr. Symptoms ceased and provocative tests with secretin and calcium have remained normal. Three additional patients with Zollinger-Ellison syndrome in whom pancreatic islet-cell tumor resection alone has resulted in long-term cures have been identified. All were middle-aged men with severe diarrhea. These successes, the availability of techniques that permit early identification and localization of gastrinomas, and the advent of H2-receptor antagonists that can control gastric hypersecretion without gastrectomy must be considered in managing patients with gastrinomas. (Author abstract) (26 Refs)

37. DIAGNOSIS AND MANAGEMENT OF GASTRINOMA (ZOLLINGER-ELLISON SYNDROME).

Clain JE
Div. Gastroenterology and Internal Medicine, Mayo Clinic, Rochester, MN
Mayo Clin Proc; 57(4):265-267 1982

Comments are presented on two accompanying papers in this journal on diagnosis of gastrinoma. One study confirmed that gastrin challenge tests distinguish patients with gastrinoma from those with duodenal ulcer disease (DUD). The peak gastrin value after secretin was the best indicator rather than absolute or percentage increase over fasting serum gastrin levels. At a level of 500 picog/ml of gastrin, there was 100% separation between 25 patients with gastrinoma and 15 with DUD. (24 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

38. TUMOR-INDUCED HYPOGLYCEMIA: A RESULT OF ECTOPIC INSULIN PRODUCTION.

Shetty MR, Boghossian HM, Duftell D, Freel R, Gonzales JC
Cancer Center Northwest Community Hosp., 800 W. Central Road, Arlington Heights, IL, 60005
Cancer; 49(9):1920-1923 1982

A 73-yr-old woman with a pelvic tumor of nerve cell origin was presented with recurrent episodes of hypoglycemia was demonstrated to have inappropriately elevated plasma insulin and hypoglycemia. The tumor contained Insulin (RIA), proinsulin and secretory type of granules. Removal of the tumor promptly produced hyperglycemia. Also no islet cell tumor was found in the pancreas, suggesting the tumor as the site of ectopic insulin production. (Author abstract) (17 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

39. EFFECT OF VASOACTIVE INTESTINAL POLYPEPTIDE ON GROWTH HORMONE SECRETION IN PERIFUSED ACROMEGALIC PITUITARY ADENOMA TISSUES.

Chihara K, Iwasaki J, Minamitani N, Kaji H, Matsukura S, Tamaki N, Matsumoto S, Fujita T

Third Div., Dept. Medicine, Kobe Univ. Sch. Medicine, 7-chome, Kusunoki-cho, Chuoh-ku, Kobe, Japan

J Clin Endocrinol Metab; 54(4):773-779 1982

The effects of vasoactive intestinal polypeptide (VIP), dopamine, and somatostatin (SRIF) on GH secretion were examined in vitro in perifused pituitary adenoma tissues obtained at surgery from seven patients with acromegaly. The perifusion of VIP at 5 x 10(-8) M resulted in a significant increase in effluent GH levels in five of the seven adenomas. A dose-related GH response was observed from 5 x 10(-9) to 5 x 10(-7) M VIP in two adenomas examined. SRIF at 5 x 10(-8) to 10(-7) M suppressed not only baseline secretion of GH but also inhibited GH rises elicited by VIP in six of the seven adenomas. Dopamine at 5 x 10(-7) to 5 x 10(-6) M decreased the baseline secretion of GH in six of the seven adenomas. In four of the six adenomas responsive to dopamine, dopamine suppressed VIP-induced GH release when perifused simultaneously. In the remaining two dopamine-sensitive adenomas in which VIP alone failed to affect GH release, the inhibition by dopamine of GH release was blocked by VIP perifused concomitantly with dopamine. Synthetic TRH or theophylline perifused at the end of the experiment stimulated GH release in all of the adenomas, indicating the viability of tumor cells throughout the study. These results suggest that VIP stimulates GH release by its direct action on pituitary adenoma cells of acromegalic patients and that VIP, SRIF, and dopamine interact at the pituitary level in modulating GH secretion from these adenomas. (Author abstract) (32 Refs)

40. THE EFFECT OF PROLACTIN ON HUMAN ALDOSTERONE-PRODUCING ADENOMAS IN VITRO.

Carroll JE, Campanile CP, Goodfriend TL

William S. Middleton Veterans Admin. Hosp., 2500 Overlook Terrace, Madison, WI, 53705

J Clin Endocrinol Metab; 54(4):689-692 1982

There is evidence for an unidentified aldosterone-stimulating factor of pituitary origin. We measured the effect of ovine PRL (oPRL) on aldosterone secretion by isolated cell suspensions of human aldosterone-producing adenomas (APAs) and compared it to the effects of angiotensins, ACTH, and potassium (K+). In the first APA, the aldosteronotropic action of large doses of oPRL was double that of angiotensin II (AII); the response to ACTH was triple that to AII, while K+ had a small stimulatory effect. Results with the second APA showed that physiological concentrations of oPRL caused a response nearly double that to AII, but, once again, less than the response to ACTH; K+ was inert. ACTH contamination of the oPRL preparation was too minute to account for these findings. We conclude that oPRL possesses aldosterone-stimulating activity in APAs greater than that of angiotensins and potassium, but less than that of ACTH. These data suggest a role for PRL in aldosterone secretion by aldosterone-producing adenomas. (Author abstract) (19 Refs)

41. SUBHYPOTHALAMIC GRAFTS OF HUMAN PITUITARY ADENOMAS IN TOTAL-BODY IRRADIATED RATS.

Landolt AM, Barker M, Deen DF, Wilson CB

Dept. Neurological Surgery Editorial Office, Univ. California, 350 Parnassus, Suite 807, San Francisco, CA, 94143

Cell Tissue Res; 221(2):269-277 1981

Human pituitary adenomas proliferate neither in cell culture nor in athymic 'nude' mice. We propose that one or several of the humoral factors necessary for the growth of pituitary adenomas is missing in these experimental environments. The purpose of our experiments was to examine the possible influence of the hypothalamus in supporting cellular proliferation, and thus adenoma growth. Fragments from four human pituitary adenomas (three pituitary prolactinomas; one ACTH-secreting adenoma) were transplanted into the pituitary fossa of total-body irradiated, hypophysectomized rats. The rats were killed after 2 wk and perfused with a mixture of formalin and India ink. Histologic examination of serial sagittal sections through the pituitary fossa and the adjacent brain showed: vascularization of the grafts from the pituitary stalk and from the scar tissue in the sphenoid bone; survival of some adenomas; and numerous mitoses in an ACTH-secreting specimen obtained from a patient who had Cushing's disease. We conclude from these experiments that as yet unidentified hypothalamic factors are essential for the growth of certain types of pituitary adenomas. (Author abstract) (21 Refs)

42. RECEPTOR FOR 1,25-DIHYDROXYVITAMIN D3 IN GH3 PITUITARY CELLS.

Haussler MR, Manolagas SC, Deftos LJ

Dept. Biochemistry, Coll. Medicine, Univ. Arizona. Tucson, AZ, 85724

J Steroid Biochem; 16(1):15-19 1982

To determine if receptors for 1,25-dihydroxyvitamin D3 have a regulatory role in specific pituitary cells, two cell lines derived from pituitary tumors were examined. Cytosol prepared from the GH3 rat pituitary tumor cell line, which produces growth hormone and prolactin in approximately equimolar ratios, was found to contain a receptor-like macromolecule that bound 1,25-dihydroxyvitamin D3 with specificity and high affinity (Kd = 2.9 x 10(-10) M). The GH3 cytosolic binding component sedimented at 3.3S in high-salt sucrose gradients and adsorbed to DNA-cellulose. Its elution profile from DNA-cellulose and other biochemical properties were indistinguishable from those of classical 1,25-dihydroxyvitamin D3 hormone receptors. The receptor was not present in the AtT-20 mouse pituitary tumor cell line, which elaborates ACTH, beta-endorphin, and beta-lipotropin. Results suggest that 1,25-dihydroxyvitamin D3 may have a central regulatory action on pituitary hormones that affect vitamin D metabolism. (28 Refs)

43. GLUCOCORTICOIDS DOWN-REGULATE SOMATOSTATIN RECEPTORS ON PITUITARY CELLS IN CULTURE.

Schonbrunn A

Lab. Toxicology, Dept. Physiology, Harvard Sch. Public Health, Boston, MA, 02115

Endocrinology; 110(4):1147-1154 1982

Treatment of GH4C1 cells, a clonal strain of rat pituitary tumor cells which synthesize and secrete PRL and GH, with 5 x 10(-6) M cortisol caused a time-dependent decrease in [125I-Tyr1]SRIF-specific binding. Receptor affinity was the same in control and cortisol-pretreated cells, but the number of SRIF-binding sites decreased from 21,900 to 15,200 receptors/cell. Pretreatment of cells with 5 x 10(-7) M dexamethasone (1,4-pregnadien-9-fluoro-16alpha-methyl 11beta,17alpha,21-triol-3,20-dione) for 43 hr caused the same maximal decrease in [125I-Tyr1] somatostatin (SRIF)-specific binding as 5 x 10(-6) M cortisol; however, dexamethasone was 10x more potent than cortisol. Pretreatment of GH4C1 cells for 43 hr with 5 x 10(-6) M 17beta-estradiol, 17alpha-methyltestosterone, testosterone, or progesterone had no effect on [125I-Tyr1]SRIF-specific binding, indicating that this effect was glucocorticoid specific. Treatment of GH4C1 cells with both dexamethasone and cycloheximide caused the same decrease in [125I-Tyr1]SRIF-specific binding as did either agent alone. In contrast, the down-modulation of SRIF receptors by chronic TRH treatment was previously shown to be additive with cycloheximide. However, maximal concentrations of TRH and cortisol added together had no greater effect on SRIF receptors than TRH alone. Therefore, even though the effects of TRH and cortisol are differentially sensitive to cycloheximide, the pathways by which they down-regulate SRIF receptors probably overlap at a common rate-limiting step. In conclusion, the receptors for TRH and SRIF are modulated in opposite directions on GH4C1 cells by chronic glucocorticoid treatment. Since these two hypothalamic peptides have opposing effects on hormone release, such receptor modulation may play an important role in regulating pituitary responsiveness to these hypothalamic regulatory factors. (45 Refs)

44. IMMUNOCHEMICAL AND BIOLOGICAL CHARACTERIZATION OF CALCITONIN ORIGINATING FROM TRANSPLANTED MEDULLARY THYROID CARCINOMA IN RATS.

Myhre L, Ekeland A, Gautvik KM
Dept. Physiology and Biochemistry, Dental Faculty, Univ. Oslo, Oslo, Norway

Acta Endocrinol (Copenh); 99(3):397-403 1982

The immunoreactive and biological activities of calcitonin (CT) produced by transplanted rat medullary thyroid carcinomas (CT) produced by transplanted rat medullary thyroid carcinomas (MCT) have been studied. Immunoreactive CT (iCT) in serum and in MCT tissues of rats carrying tumors of generations 5-8 was characterized by gel filtration on Sephadex G-100 followed by radioimmunological measurements using region specific antiserum. The hypocalcemic effect of sera and tumor extracts was tested in a rat bioassay. Rats with transplanted MCT of the fifth and sixth generations had mainly (70-84%) circulating iCT species of molecular size comparable to intact hormone. However, in rats with tumors of the seventh and eighth generations corresponding circulating iCT forms comprised less than 52% of total immunoreactivity while 32-38% eluted earlier. In comparison, iCT corresponding to intact hormone represented 30-50% of total immunoreactivity in the tumor extracts and no differences were observed between the generations. Sc injections of sera from MCT rats and of tumor extracts reduced the serum levels of ionized calcium in test rats. The sera containing mainly intact iCT showed the strongest biological potency. We conclude that rat MCT transplanted under the kidney capsule is able to secrete biologicaly active CT. However, the heterogeneity of circulating iCT increases in rats with transplanted tumors of older generations, approaching the heterogeneity of stored hormone in the gland. (Author abstract) (35 Refs)

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ENDOCRINE TUMORS

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. COMPUTED TOMOGRAPHIC DEMONSTRATION OF THE EFFECTS OF BROMOCRIPTINE ON PITUITARY MICROADENOMA SIZE.

Bonneville JF, Poulignot D, Cattin F, Couturier M, Mollet E, Dietemann JL
Dept. Neuroradiology, Univ. Hosp. Besancon, 25030 Besancon, France
Radiology; 143(2):451-455 1982

A group of 17 strictly intrasellar prolactin-secreting pituitary adenomas between 2 and 9 mm in size was examined by com-

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puted tomography before and after bromocriptine therapy of 3 mo to 1 yr duration. These findings were compared with clinical and biological data. Bromocriptine therapy was effective clinically and biologically in 14 of the 17 cases. Of the 15 intrasellar adenomas in nonpregnant patients treated with bromocriptine, 6 disappeared completely with normalization of the pituitary appearance, 5 decreased approx 50% in volume, (3 showed an increase in density, 2 a decrease), and 4 remained unchanged in size (2 showed increased density, 2 showed very low densities). (Author abstract) (13 Refs)

2. ELECTRON MICROSCOPIC STUDY OF HUMAN PROLACTIN PRODUCING PITUITARY ADENOMA.

Shimizu T, Kimura R, Tamura M, Takede F
Dept. Neurosurgery, Gunma Univ., Maebashi 371, Japan
Neurol Med Chir (Tokyo); 21(12):1219-1228 1981

An electron microscopic study of 15 cases (14 female, 1 male) of prolactin-producing pituitary adenomas was performed. All of the female patients manifested galactorrhea. Nine patients harbored intrasellar microadenoma, and the others harbored large tumor masses showing suprasellar extension. The age distribution was from 20 to 70 yr, with an av of 25.7 yr for the microadenoma-group and an av of 42.7 yr for the large tumor-group. Electron microscopic observations of adenomas obtained from 11 patients who had not received bromocriptine revealed adenoma tissue composed of polyhedral adenoma cells. The findings suggest an increased cellular activity of the adenoma cells in hormone synthesis and release. No difference in the fine structures was noticed between the microadenomas and large tumors. Bromocriptine was given preoperatively in three cases, and the serum prolactin levels were markedly reduced. In two cases, the secretory granules were increased in number and accumulated within the cytoplasm. In the other case the secretory granules decreased in number and frequently were hardly observed. The findings in bromocriptine-treated cases suggest that the drug acted to reduce the cellular activity in both hormone synthesis and release. The remaining case clinically showed the galactorrhea-amenorrhea syndrome, but an electron microscopic study disclosed a fine structure similar to that of the non-functioning adenoma. The ultrastructural findings in this particular case suggest an interference in production, release and transport of PIF by suprasellar extension of the adenoma. Electron microscopy is an essential tool in establishing the final diagnosis of prolactin-producing adenomas of the pituitary. (31 Refs) (In JPN)

3. TRANSSPHENOIDAL MICROSURGICAL REMOVAL OF GROWTH HORMONE-SECRETING PITUITARY ADENOMAS.

Baskin DS, Boggan JE, Wilson CB
Dept. Neurological Surgery, Editorial Office, Univ. California Sch. Medicine, 350 Parnassus Ave. Suite 807, San Francisco, CA, 94117
J Neurosurg; 56(5):634-641 1982

A series of 137 patients with growth hormone (GH)-secreting pituitary adenomas were treated by transsphenoidal surgery during a 10-year period. Group A comprised patients for whom this surgery was the first therapeutic intervention, and Group B included those who underwent the surgery after previous therapeutic intervention. The results were analyzed considering preoperative and postoperative endocrinological, neurological, ophthalmological, and neuroradiological data. Remission was defined as clinical response and a normal postoperative GH level, and partial remission as clinical response and postoperative reduction of the GH level by more than 50%. Any other result was considered failure. The mean follow-up period was 37.1 months; follow-up review was achieved in all the patients. Among the 120 patients in Group A, remission was achieved in 80 (78%) patients with transsphenoidal surgery alone, and in an additional 16 (16%) after postoperative irradiation (combined response rate, 94%). All failures and patients with partial remission had preoperative GH levels of more than 50 ng/ml and suprasellar extension of the tumor. There were no deaths; 8% of patients had minor surgical morbidity; 5% had new hypopituitarism postoperatively. Of patients subsequently irradiated, 71% developed hypopituitarism. Among the 35 patients in Group B, remission was achieved in 26 (74%), partial remission was obtained in 2 (6%), and 7 (20%) were considered treatment failures. There were no deaths, and the morbidity rate was 14%; 66% of patients had hypopituitarism postoperatively. Of the eight patients who had received prior irradiation only, seven (88%) went into remission. All failures and partial responders had preoperative GH levels greater than 40 ng/ml; 56% had suprasellar extension. These results confirm the efficacy of the transsphenoidal approach for the treatment of GH-secreting pituitary adenomas. (Author abstract) (49 Refs)

4. MENINGIOMA AS A SEQUEL OF RADIOTHERAPY FOR PITUITARY ADENOMA.

Spallone A
Istituto di Neurochirurgia, Universita di Roma, Viale dell' Universita 30, 00185 Roma, Italy
Neurochirurgia (Stuttg); 25(2):68-72 1982

Meningioma was found in two patients after radiotherapy for pituitary adenoma. A 38-yr-old woman presented with decreasing vision and obesity. Chromophobic adenoma had been surgically treated 9 yr prior to presentation. Radiotherapy had been given postoperatively (2,500 R) and after recurrence 7 yr later (4,100 R in 18 fractions over 3 wk). Clinical examination showed increased body hair, severe visual impairment, bilateral optic atrophy, and temporal hemianopia. A small prefrontal lobectomy was followed by removal of a large, recurrent chromophobic adenoma arising from the sella. Following surgery symptoms improved. The patient was hospitalized 11 yr later for auditory hallucinations. Two yr later the patient presented with frontal headache, visual deterioration, and a tremor in the left hand. A fibroblastic meningioma was completely removed from the sella. A 35-yr-old woman presented with oligomenorrhea and acromegaly of 13 yr duration. Radiotherapy (4,000 R over 4 wk followed after 3 mo by 2,200 Rad over 2 wk) 12 yr prior to presentation had temporarily relieved the symptoms. X-rays showed an enlarged sella with erosion of the floor. An eosinophilic adenoma was removed by transsphenoidal microsurgery. The patient returned the following yr with headache and blurred vision. A fibroblastic meningioma was removed from the floor of the anterior fossa. Review of 192 cases of pituitary adenoma suggests a causal relationship between radiotherapy and subsequent development of meningioma. (59 Refs)

5. GLYCOPROTEIN HORMONE ALPHA-SUBUNIT SECRETION IN PATIENTS WITH PITUITARY ADENOMAS: INFLUENCE OF TRH, LRH AND BROMOCRIPTINE.

MacFarlane IA, Beardwell CG, Shalet SM, Ainslie G, Rankin E
Dept. Endocrinology, Christie Hosp., Manchester, England
Acta Endocrinol (Copenh); 99(4):487-492 1982

Twelve patients with pituitary adenomas and increased serum concentration of the glycoprotein hormone alpha-subunit were studied. Eight patients were acromegalic and one had a FSH producing tumor. The adenomas in 9 patients had undergone subtotal operative removal and/or external irradiation but no patient was studied within 3 mo of these treatments. Many of the acromegalic patients, with moderately elevated alpha-levels, showed marked increases in alpha-concentration after TRH and/or LRH, compared with controls. The non-acromegalic patients, with the highest alpha-levels, showed poor responses to releasing hormones. These results suggest that excessive alpha-subunit secretion in acromegalic patients is often under hypothalamic control whereas in non-acromegalic patients it is often autonomous. Seven patients, 4 with acromegaly, were then given oral bromocriptine, 5 mg over 3 hr. There was significant fall in log mean alpha-level at 4 and 5 hr (p less than 0.02). Six patients took bromocriptine for 1-2 mo. Log mean alpha-concentration was significantly reduced at the end of treatment (p less than 0.02) and then recovered to basal levels after stopping treatment for one wk. Alpha-subunit hypersecretion in some patients with pituitary adenomas is therefore modulated by dopaminergic control mechanisms. (Author abstract) (12 Refs)

6. THE MANAGEMENT OF PROLACTIN-SECRETING PITUITARY TUMORS.

George SR, Burrow GN
Toronto General Hosp., 101 College St., Toronto, Ontario M5G 1L7, Canada
J Endocrinol Invest; 4(4):459-467 1981

Over 40% of pituitary tumors secrete prolactin. Presumptive diagnosis is based on exclusion of other causes of hyperprolactinemia, the presence of hypothyroidism, chronic renal failure, stalk section, hypothalamic space-occupying or infiltrative lesions, and neuroradiological demonstration of a pituitary fossa abnormality. Treatment may be surgical, radiologic, or chemotherapeutic, or a combination of these. The transsphenoidal approach is the surgical approach of choice. Indications for surgical treatment and evaluation of results are discussed. Years may be necessary for effects of radiation treatment to become apparent. Medical treatment may be with dopamine agonists. Bromocriptine is effective for treatment of hyperprolactinemic amenorrhea, galactorrhea and the associated hypogonadism. An approach to patients with prolactin-secreting adenomas is proposed. Proper therapy requires information about the size of the tumor, associated symptoms and signs, and the desires of the patient regarding fertility. Bromocriptine is being used more often in both patients with microadenomas and those with macroadenomas. Bromocriptine may also be useful in improving resectability of tumors preoperatively. (71 Refs)

7. ANTERIOR COMMUNICATING ARTERY ANEURYSM ASSOCIATED WITH HUGE CALCIFIED PITUITARY ADENOMA.

Wada M, Takahashi K, Hasegawa T, Abe Y, Ishii S
Dept. Neurosurgery, Juntendo Univ. Sch. Medicine, Tokyo, Japan
No Shinkei Geka; 10(2):215-220 1982

An unusual case is reported in which anterior communicating artery (A-Co-A) aneurysm was associated with huge calcified pituitary adenoma. A 59-yr-old woman was admitted to the Fujisawa City Hospital because of a sudden onset of headache with nausea which was proved to be SAH by lumbar puncture. Neurological examination revealed a somewhat disoriented patient with mild nuchal stiffness. Her optic fundi were atrophic bilaterally and she had diminished visual acuity with temporal hemianopia of the right eye. Neuroradiological studies, including skull x-ray film, cerebral angiogram and CT scan revealed ruptured A-Co-A aneurysm associated with intrasellar calcified tumor extending to the suprasellar region. Through the left fronto-temporal craniotomy, successful clipping of the neck of the aneurysm and partial removal of the tumor were made. Microscopically the specimen showed laminated calcospherites surrounded by small round or cuboidal cells with ovoid nuclei which yielded pathological diagnosis of calcified chromophobe adenoma. Brief discussion is made on both coexistence of aneurysm and brain tumor and etiology of the calcified pituitary adenoma. (Author abstract) (19 Refs) (In JPN)

8. THE ASSOCIATION OF A TUMOUR OF THE POSTERIOR PITUITARY GLAND WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 1.

Tuch BE, Carter JN, Armellin GM, Newland RC
(c/o Carter) Endocrinology Unit, Concord Hosp., Concord, NSW 2139, Australia
Aust NZ J Med; 12(2):179-181 1982

A case of multiple endocrine neoplasia (MEN) syndrome Type 1 is reported in which multiple adenomas of the parathyroid glands and islets of Langerhans were associated with a large granular cell myoblastoma of the posterior lobe of the pituitary. This rare form of pituitary pathology occurring with the MEN Type 1 syndrome appears to be unique. (Author abstract) (20 Refs)

9. AN UNUSUAL MANIFESTATION OF A PINEAL TUMOR.

Lumenta C, Bettag W
Moorenstr. 5, Dusseldorf, W. Germany
Neurochirurgia (Stuttg); 25(2):62-65 1982

Of 186 patients with brain tumors, 10 had tumors of the pineal region. A 36-yr-old man, had presented after becoming ill with motor disorders of the left side of the body and visual disorders of the left side of the field of vision of both eyes. At admission to the hospital the patient had generalized epilepsy. No neurological deficits were found. Axial cranial computerized tomography indicated a tumor in the pineal region with a cystic extension into the right temporo-occipital region. Surgery was performed using a parieto-occipital approach. Sixty-five ml of bluish-green fluid were drained from the cyst, and 15 ml of fluid were drained from an old hematoma located in the pineal region. Excision of the tumor was macroscopically complete. No postoperative complications occurred. The patient resumed his normal occupation. The only neurological sequela was a left-sided homonymous hemianopia. Histological diagnosis was pineocytoma. Of the other nine patients (4 men and 5 women, 11-58 yr old), four had astrocytomas, two had metastases of mammary carcinoma, one a metastasis of a bronchial carcinoma, one a glioma, and one a calcified cholesteatoma. Six patients died postoperatively. Three patients were alive with minimal neurological effects at the time of reporting. (26 Refs) (In GER)

THYROID TUMORS

10. ULTRASONIC DIFFRACTION SCANNING OF THE THYROID.

Merton J, Nicholas D, Hill CR, Grover S, Queenan M, Cosgrove D
Dept. Physics, Inst. Cancer Res., Belmont, Sutton, Surrey, England
Ultrasound Med Biol; 8(2):145-153 1982

Results of a preliminary clinical assessment (52 patients) of ultrasonic (US) diffraction analysis in the diagnosis of thyroid pathology are presented. Four hundred seventeen diffraction scans were randomly taken in areas that appeared abnormal on x-rays and/or grey-scale US scans. A 95% accuracy, predicted by multigroup discriminant analysis, was found when US diffraction scanning was used to separate normal and abnormal pathologies. Individual pathologies, eg, follicular adenoma, degenerating follicular adenoma and colloid masses were separated using this technique. Of 52 patients, histological reports on 23 were obtained following surgery; values for Fourier transformation patterns of diffraction scans for the latter were compared with scans from normal volunteers. Correct classification of pathologies and normal subjects was possible in 88% of cases with follicular adenomas, degenerating follicular adenomas, and colloid masses; 72% were correctly diagnosed when fetal adenoma was considered. These findings support earlier data on liver pathologies and confirms the potential of diffraction analysis for objective in vivo categorization of histopathology. (15 Refs)

11. NUCLEAR MEDICINE OF THE THYROID.

Kinoshita F
Tokyo Metropolitan Ohkubo Hosp., 2-44-1 Kabuki-cho, Shinjuku-ku, Tokyo 160, Japan
Radioisotopes; 31(1):44-54 1982

Diagnosis and treatment of thyroid diseases were discussed. Diagnosis of thyroid diseases involves the determination of the radioisotopic absorption rates of the thyroid. In this process, selection of the appropriate radioisotope (RI), pretreatment methodology, method of administering the RI and of measuring the RI absorption rates must be considered. In the case of thyroid scintigrams, 201TlCl has been used to image cancer of the thyroid gland. However, while high accumulation of the RI is observed in cases of papillary or filter cell adenocarcinoma of the thyroid, 50-70% of the cases of benign tumors also show positive findings, thus making differential diagnosis difficult. Even so, 201TlCl was thought to be the best RI for imaging papillary or filter cell adenocarcinoma, 123I or 131I are the best for investigating metastatic thyroid cancer, and 67Ga-citrate is the best for diagnosing anaplastic carcinoma and malignant lymphoma of the thyroid. 131I (100 milliCi units) has been used to treat thyroid cancer, particularly metastatic cancer, but management of the excreted RI has limited its effectiveness. The possibility of complications such as leukemia, thyroid cancer, and cancer of other organs, necessitates the use of RI. Studies of 484 children treated with 131I have not shown increased incidence of genetic anomalies. (2 Refs) (In JPN)

12. SCINTIGRAPHIC STUDIES IN PATIENTS WITH MEDULLARY CARCINOMA OF THE THYROID.

Rasmusson B
Onkologisk afd., Herlev Hosp., DK-2730 Copenhagen, Denmark
Eur J Nucl Med; 7(4):150-151 1982

Preoperative thyroid scintiscans were performed in 29 patients with medullary carcinoma (MC) of the thyroid and the results were compared with findings from palpation and pathological examination. Findings were also compared with 111 preoperative scintiscans obtained from patients with papillary (PC), anaplastic (AC), or follicular (FC) carcinomas. Isotopes used included 99mTc, 131I, and 67Ga. Cold areas corresponding to palpable MC tumors were observed in 15/29 thyroid scintiscans. Of 10 patients with normal scintiscans, 6 had palpable tumors measuring 1.5-8 cm in diameter and 4 had tumors that were either not palpable or were not apparent in the removed gland. In most groups of thyroid carcinomas, cold tumors were seen. Atypical uptake was observed in 16% of tumors. Normal uptake in palpable tumors was very high in MC compared with other thyroid tumors. Of 62 PC, 39 tumors were cold a 10 had abnormal uptake. Of 32 AC patients, 29 had cold nodules and 3 had abnormal uptake. Of 17 FC patients, 11 had cold nodules and 5 abnormal uptake. Gallium scintiscans were performed in nine patients; six had extensive tumors, but 67Ga accumulation was observed in only one. These results demonstrated that, except for MC, only 0-6% of palpable tumors greater than 2 cm in diameter had normal scintiscans; 19% of MC had normal scintiscans. Thus, 67Ga scintiscan has limited application in diagnosis of MC of the thyroid. (11 Refs)

13. DIAGNOSIS OF FOLLICULAR THYROID CARCINOMA.

Pabst HW, Dirr W
Nuklearmedizinische Klinik und Poliklinik rechts der Isar, Technischer Universitat, Ismaningerstrasse 22, D-8000 Munchen 80, W. Germany
Praxis; 71(13):555-561 1982

Carcinoma of the thyroid (CT) was diagnosed in 548 patients in the endemic goiter region of Munich. The predominant type was follicular carcinoma (FC: 47%). The male : female ratio was 1:3 for FC and 1:2.3 for all types of CT. Age distributions for CT and FC showed peaks in the range 60-70 yr old. The age distribution for papillary carcinoma showed a peak in the range 20-30 yr old. Tumor Stage I and IV each accounted for 41% of cases at diagnosis. In 24.3% of cases patients presented because of symptoms related to pulmonary or bone metastases. Prior myelography with iodine-containing contrast media for evaluation of other indications made treatment with radioiodine impossible in some cases. Metastases occurred in approx. 50% of cases. Survival rate was related to tumor stage. For Stage I and II the 50% survival rate was nearly 18 yr. Early diagnosis was a critical factor in prognosis. Distant metastases were present at diagnosis in 41% of patients. Following clinical examination the first diagnostic procedure was scintigraphy (SG). SG indicated cold nodes in 75.5% of cases, hot nodes in 5.5%, and no abnormality in 19%. Because surgical exploration of all abnormal nodes is not practical in an endemic region, cytological examination, combined with techniques of nuclear medicine provided the best diagnostic procedure. Diagnostic accuracy was 87.5% with cytological examination. (8 Refs) (In GER)

14. THE IMPORTANCE OF EARLY DIAGNOSIS IN PATIENTS WITH HEREDITARY MEDULLARY THYROID CARCINOMA.

Wells SA, Baylin SB, Leight GS, Dale JK, Dilley WG, Farndon JR
Dept. Surgery, Washington Univ. Sch. Medicine, Barnes Hosp., 4960 Audubon Ave., St. Louis, MO, 63110
Ann Surg; 195(5):595-599 1982

Ninety-two patients from 12 kindreds with hereditary medullary thyroid carcinoma (MTC) were evaluated. We sought to determine if the stimulated plasma calcitonin (CT) level at the time of diagnosis was of prognostic significance. The patients were divided into four groups according to their preoperative stimulated plasma CT levels (1) 250-1,000 pg/ml (n = 25); (2) 1,000-5,000 pg/ml (n = 36); (3) 5,000-10,000 pg/ml (n = 8); (4) greater than 10,000 pg/ml (n = 23). Compared between the four groups were several parameters, including incidence of regional lymph node metastases, incidence of residual MTC post-thyroidectomy (as indicated by increased (greater than 300 pg/ml) plasma CT levels after operation), incidence of distant metastases, and incidence of death. Also compared were the incidences of microscopic or gross MTC in thyroidectomy specimens. The incidence of regional lymph node involvement ranged from a minimum of one (4%) of 25 patients in Group 1 to 13 (57%) of 23 patients in Group 4. Similarly, plasma CT levels were elevated in only one (4%) of 25 patients in Group 1 compared to 14 (61%) of 23 patients in Group 4. There was no evidence of distant metastases or death in the patients in Groups 1, 2, or 3. In the 23 patients in Group 4, however, four (17.4%) had distant metastases and two (8.7%) died of disease during the period of observation. Of the 25 patients in Group 1, MTC was evident only by microscopic examination in 14 (56%). Eleven (44%) of the patients in Group 1 had macroscopically evident medullary thyroid carcinoma. This is in contrast with patients in Group 4 where all 23 had grossly evident MTC. These data indicate that the stimulated plasma CT level at the time of diagnosis is an excellent prognostic indicator of the extent of a disease in patients with hereditary MTC. Aggressive screening of kindred members at risk of critical importance for establishing the diagnosis and instituting therapy at a time when the neoplasm is confined to the thyroid gland. (Author abstract) (8 Refs)

15. ANAPLASTIC CARCINOMA OF THE THYROID: EARLY CLINICAL AND HISTOPATHOLOGICAL STAGES. THERAPEUTIC IMPLICATIONS.

Navarro A, Otegui I, Grezzi de Puppo S, Avellanal R, Muse IM, Garra P, Ponasso H, Reisenweber N

Clinique d'Endocrinologie et de Metabolisme, Faculte de Medecine de Montevideo, Montevideo, Uruguay

Sem Hop Paris; 58(15):895-901 1982

Anaplastic carcinomas of the thyroid (ACT) developed in 10 patients (2 men, 8 women; 27-75 yr old) secondary to thyroid nodules and multinodular goiter. Seven of the patients showed the clinical characteristics and fatal progression characteristic of ACT; histopathologically, the tumors in these patients showed differentiated zones within an anaplastic network. The tumors in the three other patients showed varying degrees of transition, clinically and histologically, in stages of differentiation and anaplasia and were associated with a more favorable prognosis. A female predominance for ACT was observed. Most cases of ACT occurred in patients between 65 and 75 yr of age. In six of the patients of the first group, pre-existing uninodular (5 patients) or multinodular (1 patient) goiter had been observed. The period of time between observation of goiter and the development of cancer was generally several yr; the period was only 5-6 mo for two of the patients. Characteristics of the malignant transformation of thyroid nodules into ACT are described. In the three transitional cases, goiter had been present for 20-30 yr in one and for 1 yr or less in the other two. Scintigraphically, all of the early nodules were cold. Differential histopathological diagnosis of ACT and medullary thyroid carcinoma is discussed. (25 Refs) (In FRE)

16. THYROGLOBULIN IMMUNOHISTOCHEMISTRY: NEW ASPECTS OF PATHOPHYSIOLOGY AND DIFFERENTIAL DIAGNOSIS OF BENIGN AND MALIGNANT GOITER.

Dralle H, Bocker W

Zentrum Chirurgie, Klinik fur Abdominal- und Transplantationschirurgie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, W. Germany

Langenbecks Arch Chir; 356(3):205-212 1982

Aspects of thyroglobulin immunohistochemistry (TGIHC) are described. TGIHC uses tissue samples fixed in formalin and imbedded in paraffin and is capable of demonstrating the functional status of benign and malignant thyroid alterations. TGIHC allows differentiation of goiters and thyroid adenomas and metastases of thyroid or other adenocarcinomas and provides information for planning of radioiodine therapy (RIT) and control of therapy. Examination of tissues indicates that nontoxic goiter develops by thyroid stimulating hormone (TSH)-dependent conversion of active thyroid follicles into inactive follicles. Inactive follicles become aggregated to form macrofollicles. Active follicles may become independent of TSH, becoming autonomous. The final stages of nontoxic goiter are probably irreversible. Thyroid adenomas include 'hot' and 'cold' nodes. Hot, endocrinologically active nodes include autonomous adenomas. Cold nodes include other main cell adenomas and differentiated adenomas, such as oxyphilic and clear-cell adenomas. In examining metastases positive TGIHC indicates that the primary tumor is a thyroid carcinoma; negative results indicate a primary adenocarcinoma of some other origin. The intensity of thyroglobulin synthesis (TGS), as indicated by TGIHC, facilitates planning of RIT, since TGS correlates with uptake of radioiodine. (16 Refs) (In GER)

17. MEDULLARY DIFFERENTIATION OF ANAPLASTIC THYROID CARCINOMA.

Nieuwenhuijzen Kruseman AC, Bosman FT, Van Bergen Henegouw JC, Cramer-Knijenburg G, De la Riviere GB

Dept. Endocrinology, St. Bartholomew's Hosp., West Smithfield, London

Am J Clin Pathol; 77(5):541-547 1982

Fourteen cases of anaplastic carcinoma of the thyroid (ACT) were studied with silver staining and immunohistochemical technics for signs of medullary differentiation. For comparison a series of 11 cases of medullary carcinoma of the thyroid (MCT) was studied. In 9 out of 14 cases of ACT both argyrophilia and immunoreactive calcitonin could be detected as evidence of an apparent C-cell origin of these tumors. Most of the patients with these anaplastic medullary carcinomas died within 6 months after the histological diagnosis was made. It is concluded that the histological diagnosis of anaplastic variants of MCT can only be made on the basis of argyrophilic cytoplasmic granules and calcitonin immunoreactivity. In contrast to well differentiated MCT the anaplastic medullary carcinoma is characterized by a poor prognosis. (Author abstract) (33 Refs)

18. RADIOIODINE THERAPY OF FOLLICULAR THYROID CARCINOMA.

Dirr W, Pabst HW
Nuklearmedizinische Klinik und Poliklinik rechts des Isar, Technische Universitat, Ismaningerstrasse 22, D-8000 Munchen 80, W. Germany
Praxis; 71(13):562-566 1982

Radioiodine therapy (RIT) of follicular thyroid carcinoma is described. The aim of RIT is elimination of tumor cells that accumulate iodine. Accumulation of radioiodine in histologically confirmed thyroid carcinoma and in some cases in metastases is an indication for RIT. Thyroid carcinomas are relatively radioresistant, requiring dose of 30,000-40,000 rad. The high radiation dose requires removal of normal thyroid tissue. Uptake of 131I by tumor cells can be stimulated by endogenous or exogenous thyroid stimulating hormone (TSH). Exogenous TSH carries the risk of allergic reaction. TSH can also block hypothalamic-hypophyseal regulation. The effective half-life of radioiodine can be extended by suppression of TSH-stimulation, achieved by substitution therapy with L-triiodothyronine. Administration of 1.8 ug/kg in fractioned doses is well tolerated. Extending the half-life of radioiodine carries the risk of damaging the bone marrow. This risk can be minimized by administration of inactive iodine. Computer tomography allows precise estimation of tumor mass, a critical factor in response to therapy. RIT produces tumor regression in approx 33% of patients with bone metastases. RIT produces complete elimination of tumor in 50% of patients with pulmonary metastases, regression in 33%, and temporary arrest of growth in the remainder. The most effective treatment of follicular thyroid carcinoma requires close cooperation of all involved medical disciplines. (6 Refs) (In GER)

19. CHEMOTHERAPY OF THYROID CARCINOMA.

Brunner K
Institut fur medizinische Onkologie, Inselspital, 3010 Bern, Switzerland
Praxis; 71(14):603-605 1982

Because of the success of surgical therapy, chemotherapy (CT) of thyroid carcinoma has not been thoroughly tested. The most effective chemotherapeutic agent is apparently Adriblastin with a remission rate of 36-55%. Early results suggest that the combination of cis-platinum and Adriblastin may be more effective. CT should be considered for patients resistant to other forms of therapy, for metastatic Hurthle-cell tumors, and for metastatic medullary carcinoma. CT should be used as adjuvant therapy after radical surgery and postoperative radiotherapy and as palliative therapy in metastatic cases. (5 Refs) (In GER)

20. THYROID CANCER: CLINICAL EXPERIENCE WITH 320 CASES SEEN IN 27 YEARS.

Lopez Caffarena E, Torres J, Dominguez M, Volpato R, Martinez V, Maira J, Rolando M, Lobo G, Galarza S, Perez G, Philippi V
Casilla 2337, Santiago de Chile, Chile
Rev Med Chil; 110(2):123-132 1982

Among 1,984 surgeries performed on thyroid gland, 320 were because of cancer. Of the 320 patients (53 men, 267 women; less than 10 to greater than 70 yr old), 173 had papillary cancer, 118 had follicular, 20 had anaplastic, 6 had medullar, and 3 had primary lymphoma; total of 291 of the patients had differentiated cancer. Scintigraphy was performed on 206 of the patients, 2 had hyperfunctioning nodules, 170 had hypofunctioning (so called cold nodules), and 34 had functioning nodules. Types of surgery performed consisted of total thyroidectomy (TH: 61), almost total TH (112), radical unilateral cervical lymphadenectomy (CLA: 66), radical bilateral CLA (8), modified CLA (7), partial resection (5), lobectomy (86), and bilateral subtotal lobectomy (40). Five patients died because of surgery, 13 developped hypoparathyroidism, and 6 had recurrent neural damage. Patients with anaplastic cancer died within 2 yr, but only one patient with medullary cancer had died. Of the 320 patients, 248 were under control, 10 were lost, and 62 died. (86 Refs) (In SPA)

PARATHYROID TUMORS

21. DEFERRED PARATHYROID AUTOGRAFTS WITH CRYOPRESERVED TISSUE AFTER REOPERATIVE PARATHYROID SURGERY.

Saxe AW, Spiegel AM, Marx SJ, Brennan MF
(c/o Brennan) Dept. Surgery, Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Arch Surg; 117(5):538-543 1982

Between August 1975 and March 1981, 12 patients underwent forearm parathyroid autotransplantation with cryopreserved tissue following reoperative parathyroid surgery. Tissue had been cryopreserved 2 to 18 mo. Follow-up ranged from 4 to 66 mo (median, 18 mo) following autotransplantation. All patients required calcium supplementation as a condition for autografting; six patients were no longer receiving calcium supplementation at most recent follow-up and in one patient the dosage was being tapered. The presence of a parathyroid hormone gradient of 2:1 or greater correlated well with freedom from calcium supplementation. Of seven patients with preautograft and postautograft urinary cyclic adenosine monophosphate (cAMP) determinations, three with increases following transplantation did not require calcium, three without increases continued to require calcium, and the patient whose dosage was being tapered had increased urinary cAMP levels. (Author abstract) (33 Refs)

22. PRIMARY HYPERPARATHYROIDISM DUE TO OVERACTIVE INTRATHYROID PARATHYROID GLANDS: A POTENTIAL CAUSE OF FAILED EXPLORATION.

Bainbridge ET, Barnes AD
Queen Elizabeth Hosp., Queen Elizabeth Medical Centre, Edgbaston, Birmingham B15 2TH, England
Br J Surg; 69(4):200-202 1982

The variable location of the parathyroid glands is a significant factor in unsuccessful cervical exploration for hyperparathyroidism. Particular difficulty may be experienced when an overactive parathyroid is concealed within the substance of the thyroid. Currently available methods of localizing abnormal parathyroid tissue may well fail to indicate an intrathyroid location. The latter possibility should always be considered whenever thorough cervical exploration has failed to reveal a parathyroid tumor as such awareness may obviate re-exploration or an unnecessary sternotomy. This report details the clinical features and operative findings in six patients whose primary hyperparathyroidism was due to an overactive intrathyroid parathyroid gland. Successful parathyroid surgery demands a strict routine exploration of the possible sites of overactive glands, virtually all of which are easily accessible through a standard collar incision. (Author abstract) (23 Refs)

23. TRANSPLANTATION HYPERPARATHYROIDISM: TUMORLIKE GROWTH AND AUTONOMOUS FUNCTION OF AUTOGRAFTS OF THE HYPERPLASTIC PARATHYROID.

Klempa I, Rottger P, Schneider M, Frei U, Koch KM
Zentrum der Chirurgie, Johann-Wolfgang-Goethe-Universitat, Theodor-Stern-Kai 7, D-6000 Frankfurt a. M. 70, W. Germany
Langenbecks Arch Chir; 356(3):191-204 1982

Forty-one patients with secondary uremic hyperparathyroidism resulting from chronic renal failure were treated by total parathyroidectomy followed by autotransplantation of parathyroid tissue into the musculature of the forearm. Parathormone levels were measured in blood drawn from the cubital vein of the transplant-bearing arm and the contralateral arm initially at 3-mo intervals and later at 6-mo intervals. Observation time was 5 yr. Transplant tumors developed in five patients within 7-33 mo of transplantation. Locally continuous and discontinuous invasion of surrounding tissue, blood vessels, and musculature by hyperplastic parathyroid tissue was found. Microscopic examination showed an increase in mitoses in hyperplastic tissue compared with normal tissue, indicating malignant character of the hyperplastic tissue. DNA histograms showed peaks for normal and hyperplastic parathyroid tissue at the diploid level. The hyperplastic tissue, however, showed a shift towards the tetraploid level. Histograms of less nodular tumors showed distinct peaks at both diploid and tetraploid levels, while in histograms of nodular tumors these peaks were less distinct. Two patients showed normal DNA values in excised parathyroid tissue but elevated levels in transplant tissue; two patients showed elevated levels in both the excised tissue and the transplanted tissue. Occurrence of hyperplasia in transplants indicates that the procedure is not justified in treatment of renal osteodystrophy. (28 Refs) (In GER)

ADRENAL TUMORS

24. COMPUTED TOMOGRAPHY STUDY OF 100 CASES OF ADRENAL GLAND DISORDERS.

Picard JD, Lacrosniere L, Bard DM, Ducellier R, Gruson B, Lubrano JM, Luton JP, Parienty R, Perez R, Pradel J, Wellers M
Scanner-Intercliniques Hartmann, Neuilly-sur-Seine, France
Bull Acad Natl Med (Paris); 165(1):57-73 1981

Computed tomography (CT) findings are presented for 100 patients with adrenal gland disorders, including 75 with adrenal hormone hypersecretion (30 pheochromocytomas, 8 Conn's adenomas, 34 metabolic hypercorticism, and 4 multi-secretory tumors), 19 with non-secreting tumors (7 primary and 12 secondary), 3 with adrenal hematomas, and 3 with adrenal insufficiency. CT diagnoses of adrenal tumors and pseudotumors were based on augmentation of one or both of the adrenal glands, homogeneity or heterogeneity of adrenals, and relationship to neighboring organs. Pheochromocytomas (PT) were characterized by regular contours and, in half of the cases, homogeneity. Of non-homogenous PT forms, 2/3 showed areas of necrosis. Of the 30 PT, 4 were malignant. CT is useful in the diagnosis of PT: false negatives are rare and false positives exceptional. Indications for CT in the diagnosis of metabolic hypercorticism include the determination of the etiology of Cushing's disease and the detection of primary or recurrent adrenal tumors. CT is of little use in defining adrenal hyperplasia related to Cushing's disease. In the cases of primary adrenal tumors, CT allows the determination of tumor location within the adrenal gland, of its relationship to neighboring organs, and of the existence of hepatic metastases. Adrenal metastases are usually bilateral and often discovered by chance. (11 Refs) (In FRE)

25. ADRENAL PHAEOCHROMOCYTOMA IN FAMILIAL NEUROFIBROMATOSIS WITH INITIAL CONTROL OF HYPERTENSION BY LABETALOL.

Stewart PA
Velindre Hosp., Whitechurch, Cardiff, CF4 7XL, Wales
J R Soc Med; 75(4):276-278 1982

The case of a 45-yr-old woman with familial neurofibromatosis is presented in whom satisfactory control of adrenal pheochromocytoma-induced paroxysmal hypertension with labetalol was achieved. The patient presented with heavy pigmentation, cafe au lait spots, small truncal and limb neurofibromata, and blood pressure fluctuations of 150/80 to 220/20 without evidence of longstanding hypertension. Oral labetalol (100 mg, six-hourly) easily controlled the hypertension. The tumor was successfully located preoperatively by iv urography, although adrenal tomography and isotope scanning were performed without success. The pheochromocytoma was also located by selective plasma noradrenaline assays at adrenal venography which showed concentrations in the right renal vein and upper inferior vena cava. Arteriography demonstrated right adrenal tumor circulation. A 5-cm diameter tumor was removed uneventfully with no other intra-abdominal tumors located at laparotomy. The patient remained well 3 yr post surgery, without sweating episodes, normotensive without medication, and with normal 24-hr urinary catecholamine concentrations. (13 Refs)

26. A DIRECT RADIOIMMUNOASSAY OF PLASMA ALDOSTERONE IN NORMAL SUBJECTS AND PATIENTS WITH HYPERTENSION OR RENAL DISEASE USING 125I-LABELED LIGAND (ALDOCTK-125 KIT).

Kawasaki T, Nakamuta S, Omae T
Second Dept. Internal Medicine, Kyushu Univ. Faculty Medicine, Fukuoka 812, Japan
Fukuoka Igaku Zasshi; 72(11):633-638 1981

Plasma aldosterone concentrations (PAC) were measured in normal subjects (25 males and 17 females) and in patients with essential hypertension (51), primary aldosteronism (PA: 10), renovascular hypertension (10), pheochromocytoma (PC:4), chronic glomerulonephritis (18), or malignant hypertension (10). The PAC was 14.7 +-4.1 ng/deciliter in the PC patients; it did not increase significantly in the PA and PC patients administered low-salt (NaCl, 2g/day) diets for 4 days. Within 4 wk after unilateral adrenalectomy, the PAC in the PA patients was almost the same as that in the PC patients on a control diet (NaCl, 10g/day), and the PAC was significantly increased by the low-salt diet. (20 Refs) (In JPN)

27. PGE2, PGF2ALPHA AND CATECHOLAMINES IN PHEOCHROMOCYTOMA.

Ignatowska-Switalska H, Wocial B, Januszewicz W, Filipecki S
Dept. Angiology, Medical Acad., Nowogrodzka 59, 02-006 Warszawa, Poland
Prostaglandins Leukotrienes Med; 8(1):37-48 1982

The urinary excretion of prostaglandin E2 (PGE2) and prostaglandin F2alpha (PGF2alpha) in relation to urinary catecholamine patterns was investigated in 14 patients with pheochromocytoma (PH). PGE2 and PGF2alpha were determined by radioimmunoassay; adrenaline (A), noradrenaline (NA), and dopamine (DA) were measured fluorometrically. The mean urinary level of PGE2, 619.9 picomole (pmol)/24hr, did not differ significantly from the control value of 1,075.0 pmol/24 hr. The mean level of PGF2alpha, 3,598.0 pmol/24 hr, was significantly higher than that in controls, 1,886.9 pmol/24 hr. In patients exhibiting elevated levels of NA + A, NA alone, and DA, urinary PGE2 was significantly decreased to 367.4, 445, and 440.4 pmol/24 hr, respectively. In patients with elevated NA + A, normal NA + A, and elevated DA, urinary PGF2alpha was significantly increased to levels of 6,375, 1,035, and 5,070 pmol/24 hr, respectively. PGF2alpha was decreased to 989 pmol/24 hr in patients with elevated A. No significant correlation was found between prostaglandin and catecholamine excretion in the whole group of patients. Only in those with normal DA was a significant inverse correlation found between excretion of PGF2alpha and DA. Thus, prostaglandin excretion is related to the pattern of catecholamine excretion in PH patients. The low PGE2 excretion in most of the patients suggests a disturbance in the physiological interrelationship between prostaglandins and catecholamines. An increased activity of the 9-keto-reductase converting PGE2 to PGF2alpha might explain the increased excretion of the latter in PH. (25 Refs)

PANCREAS TUMORS

28. ZOLLINGER-ELLISON SYNDROME: A SHIFT IN SURGICAL THERAPY: AN ANALYSIS OF 27 PATIENTS.

Klempa I, Encke A, Classen M, Feurle GE

Abteilung fur Allgemein- und Abdominalchirurgie, Zentrum der Chirurgie, Johann-Wolfgang-Goethe-Universitat, Theodor-Stern-Kai 7, D-6000 Frankfurt/Main 70, W. Germany

Chirurg; 53(4):263-269 1982

Zollinger-Ellison syndrome (ZES) was diagnosed in 27 patients. Diagnosis wa based on immunohistologic methods in 10 cases, and on phlebography using selective transhepatic catheterization of the pancreatic veins in 8 cases, of which 2 were further confirmed by immunohistological methods. Tumors included four pure gastrinomas, four mixed-type pancreatic tumors, seven multiple endocrine adenomas with hyperparathyroidism, and two multiple adenomas with insulinoma as a second tumor. In 12 patients diagnosis of gastrinoma was based on clinical findings only; no tumor was found surgically. Clinical diagnosis of ZES was based on fasting levels of gastrin of an av 1,273 picog (pg)/ml (compared with normal values up to 50 pg/ml) and a rise in gastrin levels after infusion of secretin and calcium. These findings were not significantly different between patients with surgically confirmed gastrinomas and those without surgically confirmed tumors. Gastrinomas were removed from 10 patients; five of these tumors were localized by phlebography. One patient died of tumor progression. Four patients died postoperatively. Localizing diagnostic procedures and consecutive tumor removal were made possible by the use of H2-receptor antagonists. Improvement in localizing diagnosis combined with low morbidity associated with tumor removal have led to a trend away from total gastrectomy as therapy for ZES. (35 Refs) (In GER)

29. EFFECT OF SOMATOSTATIN ON GASTRIN, INSULIN AND GLUCAGON SECRETION IN TWO PATIENTS WITH ZOLLINGER-ELLISON SYNDROME.

Fallucca F, Delle Fave GD, Giangrande L, Del Blazo L, De Magistris L, Carratu R

Cattedra di Medicina Costituzionale ed Endocrinologia, II Clinica Medica I, Policlinico Umberto 1, Viale del Policlinico, 00161 Rome, Italy

J Endocrinol Invest; 4(4):451-453 1981

Clinical symptoms of a 30-yr-old man and a 58-yr-old woman with Zollinger-Ellison syndrome (ZES) included duodenal ulcer with gastric acid hypersecretion and diarrhea. Following stimulation with secretin (SE) and bombesin (BBS), fasting gastrin, glucagon and insulin levels were reduced. During somatostatin infusion, gastrin and glucagon responses to SE and BBS were inhibited in both patients and insulin was inhibited in one. Somatostatin may be useful for diagnosis and treatment of patients with ZES. (13 Refs)

30. NEONATAL ISLET CELL ADENOMA: A DISTINCT TYPE OF ISLET CELL TUMOR?

Bordi C, Ravazzola M, Pollak A, Lubec G, Orci L

(c/o Orci) Inst. Histology and Embryology, Univ. Geneva Medical Sch., 1211 Geneva 4, Switzerland

Diabetes Care; 5(2):122-125 1982

Conventional histologic and immunofluorescence studies were performed on pancreatic fragments removed from a newborn male with persistent hyperinsulinemic hypoglycemia caused by a compact islet cell adenoma. While histologic examination revealed structure identical to that of adult islet cell adenomas, immunofluorescence revealed a complex cellular composition of tumor; four islet cell hormones were stored in different cells that showed the same spatial distribution usually seen in normal islets. (12 Refs)

GONADAL TUMORS

31. THE ROLE OF HUMAN CHORIONIC GONADOTROPIN IN SEMINOMATOUS TESTICULAR TUMOR.

Masuda M

Dept. Urology, Sch. Medicine, Kobe Univ., Japan

Hinyokika Kiyo; 28(1):1-12 1982

In order to investigate the significance of human chorionic gonadotropin (hCG) in seminoma of the testis, serum hCG levels in peripheral and testicular venous bloods before orchiectomy and hCG levels in tumor tissues were measured in 25 cases. Additionally, tissue specimens of seminomas were immunohistochemically studied for the cellular location of hCG by peroxidase antiperoxidase (PAP) method. The results were as follows: The rates of elevation of serum hCG levels were 47.8% in peripheral venous blood, and 88.8% in testicular venous blood. HCG levels in tumor tissues were detected in all cases, and their average level was 437.6 ng/g tissue. In case hCG levels in tumor tissues were less than 150 ng/g tissue, serum hCG were negative both in testicular and peripheral venous bloods. However, in case showing the level more than 150 ng/g tissue, serum hCG in testicular venous blood were positive, and if more than 200 ng/g tissue, serum hCG in peripheral venous blood were positive in all cases. By PAP method, hCG was demonstrated within syncytiotrophoblastic giant cell (STGC) in 10 of 22 cases, and in 2 cases of 10, cellular localizations of hCG were found not only in STGC but also in tumor cells of seminoma. In the positive group by PAP method, both serum hCG levels and rates of elevation of serum hCG levels in peripheral and testicular venous bloods were higher than the negative group. And the same result was obtained in hCG levels in tumor tissues. It was concluded that the measurement of serum hCG levels in peripheral venous blood before orchiectomy is useful as a serum marker for seminoma. STGC were mostly seen by PAP method in the cases which showed high hCG levels before orchiectomy among the cases diagnosed as pure seminoma histopathologically by hematoxylin-eosin stained specimens. Those should be regarded as non-seminomatous germ cell tumors. (Author abstract) (40 Refs) (In JPN)

32. HUMAN CHORIONIC GONADOTROPIN AS A MARKER FOR TESTICULAR TUMORS.

Mann K
Univ.-Klinik II, Klinikum Grosshadern, Marchioninistrasse 15, 8000 Munchen 70, W. Germany
Fortschr Med; 100(9):379 1982

Potential tumor markers were investigated in serum samples obtained from 230 patients with testicular tumors. Human chorionic gonadotropin (HCG) and alpha-fetoprotein were elevated in the serum of patients with testicular malignancies. In addition, elevated levels of HCG alpha- and beta-chains were also detected. It is suggested that radioimmunoassays of HCG could be used in primary diagnosis of malignant testicular tumors, staging, and monitoring the course of the disease and the effects of therapy. (no Refs) (In GER)

OTHER TUMORS OF GLANDULAR TISSUES

33. LACK OF CORRELATION OF A HISTOCHEMICAL METHOD FOR ESTROGEN RECEPTOR ANALYSIS WITH THE BIOCHEMICAL ASSAY RESULTS.

Panko WB, Mattioli CA, Wheeler TM
Dept. Pathology, Baylor Coll. Medicine, Houston, TX, 77030
Cancer; 49(10):2148-2152 1982

Forty-nine specimens of carcinoma of the breast were analyzed for estrogen receptor content using the sucrose gradient method and a histochemical method using a conjugate of estradiol (6-BSA-Fluor-CMO-17beta-estradiol). The specimens analyzed by the histochemical method were graded for fluorescent intensity, percentage of cells fluorescing, and cellularity. Only 53.1% (26/49) of the specimens were classified into the same three categories (positive, negative and ambiguous) as classified by the biochemical assay. If the negative and ambiguous categories were combined, the degree of correspondence rose to only 63.3% (31/49). Because the classification scheme was arbitrary and because the results of the biochemical assay might be correlated with one or more factors, univariate and multivariate analyses were used to examine the data for any underlying relationships. Only the age of the patient was significantly correlated with the results of the biochemical assay. Importantly, neither the percentage of cells fluorescing nor the fluorescent intensity was correlated with the results of the biochemical assay. Terms to account for various interactions of parameters did not enhance the association with the biochemical results. While this histochemical assay may eventually prove to be effective in selecting patients for endocrine therapy, it does not seem to be a substitute for the standard biochemical assay for estrogen receptors presently used. (Author abstract) (11 Refs)

34. THE VALUE OF REPEATING STEROID RECEPTOR ANALYSES IN THE ENDOCRINE TREATMENT OF BREAST CANCER (MEETING ABSTRACT)

Stewart JF, King RJ, Steiner R, Hayward JL, Rubens RD
Imperial Cancer Research Fund Breast Cancer Unit, London SE1 9RT, England
Proc Am Soc Clin Oncol; 1:C-283 1982

One hundred and fifty-six patients with advanced breast cancer of known estrogen receptor (ER) and progesterone receptor (PgR) status treated by endocrine therapy were studied. Regarding a value for both ER and PgR as greater than or equal to 5 fmol/mg cytosol protein as positive, patients were divided into 4 phenotypic sub-groups:- ER+PgR+ (43%), ER+PgR- (26%), ER-PgR+ (8%) and ER-PgR- (23%). Responses to first endocrine therapy for each tumor phenotype were ER+PgR+ 50%, ER+PgR-27%, ER-PgR+ 27% and ER-PgR-6%. Four of 16 (25%) patients with ER+PgR+ tumors responded to subsequent endocrine therapy, but responses were not observed for 20 tumors of any other phenotype. With ER+PgR+ tumors, responses were seen in 20/30 (67%) patients when receptors were measured on tumor recurrence or on primary tumor immediately before endocrine therapy; but in only 11/32 (32%) when receptor analysis was performed on primary tumor and endocrine therapy was started only after failure of primary local therapy. In sequential analyses of receptors a change in ER phenotype occurred in 28/104 (27%) tumors, and in PgR phenotype in 12/42 (29%). These results demonstrated that repeat steroid receptor assays immediately before endocrine therapy improve the prediction of response to treatment. (no Refs)

35. ENDOCRINE RESPONSIVENESS OR NON-RESPONSIVENESS AND SITES OF METASTATIC DISEASE IN ADVANCED BREAST CANCER (ABC) (MEETING ABSTRACT)

Ceci G, Torriani P, Passalacqua R, Rizzoli V, Cocconi G
Clinica Medica Universita, Parma 43100, Italy
Proc Am Soc Clin Oncol; 1:C-288 1982

In abc, response or non-response to the first endocrine therapy (eRx) is nearly always predictive of a general endocrine responsiveness or non-responsiveness. The records of patients (pts) with abc, seen and followed continuously in our institution and treated with at least one eRx evaluable for response, were retrospectively reviewed. Pts receiving a combination of endocrine-chemo Rx, before the first evaluable eRx, were excluded. One hundred and forty-five pts were considered evaluable. Seventy-two percent had been treated with one, 19% with two, 9% with three or more eRx. Two groups of pts were identified: group A, 68 pts. responding to at least one eRx; group B, 77 pts, non-responding to any eRx. The two groups significantly differed in actuarial free interval (median values (mv) 26 and 15 mo), survival from time of first recurrence (mv 49 and 27 mo), survival from time of diagnosis (mv77 and 49 mo). Sites of initial relapse were more commonly bone (46% vs 30%) in pts of group A than in pts of group B, more commonly liver (9% vs 1%) and significantly more commonly viscera (25% vs 7%) in pts of group B than in pts of group A. Considering all sites of metastatic disease, viscera (51% vs 29%), liver (21% vs 4%), brain (16% vs 3%), bone and viscera together (33% vs 4%), were more commonly found in pts of group B than in pts of group A. (no Refs)

36. IMMUNOREACTIVE PROLACTIN IN EPITHELIAL CELLS OF NORMAL AND CANCEROUS HUMAN BREAST AND PROSTATE DETECTED BY THE UNLABELED ANTIBODY PEROXIDASE-ANTIPEROXIDASE METHOD.

Purnell DM, Hillman EA, Heatfield BM, Trump BF
Dept. Pathology, Sch. Medicine, Univ. Maryland, Baltimore, MD, 21201
Cancer Res; 42(6):2317-2324 1982

A rabbit antiserum to ovine prolactin was used with the peroxidase-antiperoxidase method to search for immunoreactive prolactin in normal and pathological human breast and prostate. The immunostaining of pituitary cells appeared specific for prolactin since both ovine and human prolactin abolished immunostaining when they were added to the anti-prolactin serum. We stained sections of normal breast and normal prostate. Results suggested that the immunostaining of normal breast and prostate was related to the presence of immunoreactive prolactin in epithelial cells of these organs. In prostate, immunostaining was confined to the secretory cell population. In breast, immunostaining seemed to occur throughout the breast parenchyma. The immunostaining of normal breast epithelium was markedly heterogeneous. This was less pronounced in normal prostate epithelium. Sixty-four percent of the primary prostate adenocarcinomas which were examined showed strong staining reactions with anti-prolactin serum. Two of three metastatic tumors of prostate origin had similar strong staining reactions. Infiltrating duct carcinomas of the breast were strongly stained with anti-prolactin serum, but most breast fibroadenomas were not stained. None of seven adenocarcinomas of the colon tested as controls were stained by anti-prolactin serum. The results suggested that the immunostaining of breast and prostate carcinomas was related to immunoreactive prolactin. The results reported here emphasize the value of the peroxidase-antiperoxidase method in the study of hormone target organ interactions as well as in retrospective studies of pathological materials. (33 Refs)

37. IMMUNOMODULATORY EFFECTS OF OESTROGEN IN PROSTATIC CANCER: UPDATE AND FURTHER CONSIDERATION.

Ablin RJ
Div. Immunology, Cook County Hosp., Chicago, IL, 60612
Allergol Immunopathol (Madr); 9(1):63-70 1981

Recent experimental and clinical studies are reviewed which indicate that alterations of the endocrine environment may have profound effects on the immunogenicity of tumor and host responsiveness in patients with prostatic cancer (PC). A preliminary study in 123 PC patients subjected to cryosurgical prostatectomy suggested that there was a better clinical response and increased survival in those who did not receive hormonal therapy compared to those who did. Histological reactions were determined in pre- and post-surgical prostate tissue biopsies of 37 of these patients for whom there had been clinical indications for biopsy. The inflammatory reactions observed, characterized by granuloma, eosinophils (ES) and lymphocytes (LM), or plasma cells (PLC) correlated with three favorable findings: (1) superior survival, 73% (11/13) with LM or PLC and 86% (6/7) of patients with ES vs 50% survival in patients without these infiltrates; (2) infiltrates were observed only in patients with well differentiated, moderately well differentiated or cribriform patterns; and (3) the absence of cancer in 57% (4/7) of patients with ES, 47% (7/15) of patients with LM or PLC, and 1 patient with granuloma vs presence of cancer in 88% (7/8) of patients in which tissue was unchanged from pre-cryosurgical biopsies. Histological changes were also correlated with hormonal therapy (estrogens and/or orchiectomy). It is suggested that the inflammatory infiltrates might represent a local antitumor immune reaction following cryosurgery. (34 Refs)

38. GONADOTROPIN-RELEASING HORMONE ANALOGUES FOR PROSTATE CANCER: UNTOWARD SIDE EFFECTS OF HIGH-DOSE REGIMENS ACQUIRE A THERAPEUTICAL DIMENSION.

Jacobi GH, Wenderoth UK
Urologische Klinik und Poliklinik im Klinikum, Johannes-Gutenberg-Universitat, Langenbeckstrasse 1, D-6500 Mainz, W. Germany
Eur Urol; 8(3):129-134 1982

Gonadotropin-releasing hormone (Gn-RH), a hypothalamic decapeptide, mediates the synthesis and release of pituitary luteinizing hormone (LH). Synthetic Gn-RH analogues with prolonged duration of action are therapeutically administered with 'pro-fertility' intention to overcome endogenous Gn-RH deficiency, ie hypogonadotropic hypogonadism and related disorders. When Gn-RH analogues are chronically administered in high supraphysiological dosages, however, a paradoxical effect of pituitary overstimulation becomes evident: gonadotropin release is reduced, Leydig cell responsiveness is impaired, and testosterone secretion is blocked to castrate levels. Metabolic mechanisms involved include desensitization of the pituitary to Gn-RH, down-regulation of Gn-RH receptors, the depletion of the releasable LH pool, the breakdown of physiological feedback mechanisms, as well as direct interactions of the Gn-RH analogue with the Leydig cell. It is tempting to assume that, on the basis of this untoward side effect, high dose Gn-RH analogues will acquire a therapeutical dimension in the palliative treatment of prostate cancer. The therapeutical effect of castrate levels of testosterone is achieved without orchiectomy, cardiovascular side effects of estrogens are avoided, and the drug is conveniently applicable via the pernasal route. From the data available today Gn-RH analogues in overstimulatory dosage can be expected to be safe and effective in the palliative treatment of prostate cancer and would thus prove a true alternative to conventional contrasexual measures. (Author abstract) (35 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

39. GONADAL FUNCTION AFTER PLATINUM, VINBLASTINE, BLEOMYCIN (PVB) +/- ADRIAMYCIN (A) IN TESTICULAR CANCER (MEETING ABSTRACT)

Draaga RE, Williams SD, Stevens EE, Patel DN, Einhorn LH, Rohn RJ
Indiana University Hospital, Indianapolis, IN, 46223
Proc Am Soc Clin Oncol; 1:C-407 1982

Patients with disseminated testicular cancer and no prior retroperitoneal lymphadenectomy treated with PVB +/- A were evaluated with sperm counts, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone. Since 1979, 37 men have been prospectively studied. Median followup is 18 months. Before treatment, 20 of 27 were oligospermic and only

3 could meet requirements for sperm banking. FSH was elevated in 1 of 37. After two months, 17 of 18 were aspermic, 18 (100%) were oligospermic, and FSH was elevated in 16 of 29. After 1 year, 7 of 8 remain aspermic and 12 of 13 have elevated FSH. Also, 19 patients treated between 1975-1979 were retrospectively evaluated. Median followup from the start of therapy was 36 months. Normal sperm counts were found in 8 of 16. FSH was normal in 10 of 18. LH was normal in 12 of 18. Testosterone was normal in 14 of 18. Five of 17 have impregnated their wives resulting in 3 healthy babies, 1 ongoing pregnancy, and 1 spontaneous abortion. These results show that: (1) Significant impairment of spermatogenesis exists before therapy precluding the possibility of sperm banking in most patients, (2) Cisplatin-based combination chemotherapy has substantial effects on gonadal function, and (3) A high degree of recovery of spermatogenesis occurs sometime after 2 to 3 years from the initiation of treatment. (no Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

40. PROLACTIN STORAGE IN A CLONAL STRAIN OF RAT PITUITARY TUMOR CELLS IS CELL-CYCLE DEPENDENT.

Kiino DR, Burger DE, Dannies PS
Dept. Pharmacology, Yale Univ. Sch. Medicine, New Haven, CT, 06510
J Cell Biol; 93(2):459-462 1982

GH4C1 cells (GH cells) are a clonal strain of rat pituitary tumor cells which secrete prolactin. We measured intracellular prolactin at different stages of the cell cycle using flow microfluorometry. Prolactin was stained by an indirect immunocytochemical technique using fluorescein isothiocyanate (FITC)-conjugated antiserum, and DNA was stained simultaneously with propidium iodide. We found that prolactin storage in GH cells was cell-cycle dependent; prolactin storage increased as cells passed from G1 to S to G2 + M. We have shown previously that insulin and 17beta-estradiol act synergistically to increase intracellular prolactin three- to sevenfold and slow the rate of cell growth to approx 70% of control cells. In this study we observed that insulin and estradiol increased prolactin storage at each stage of the cell cycle but did not affect the cell-cycle distribution of the population even though cell growth was slowed. We conclude that insulin and estradiol did not increase prolactin storage by affecting the cell-cycle distribution of the population. (Author abstract) (13 Refs)

41. INDUCTION OF PROLACTIN-DEFICIENT VARIANTS OF GH3 RAT PITUITARY TUMOR CELLS BY ETHYL METHANESULFONATE: REVERSION BY 5-AZACYTIDINE, A DNA METHYLATION INHIBITOR.

Ivarie RD, Morris JA
Dept. Molecular and Population Genetics, Univ. Georgia, Athens, GA, 30602
Proc Natl Acad Sci USA; 79(9):2967-2970 1982

GH3 cells are a rat pituitary tumor line expressing two pituitary peptide hormones, prolactin (rPRL) and growth hormone. Recently, it was found that the DNA alkylating agent ethyl methanesulfonate can induce the appearance of rPRL-deficient GH3 cell variants at a high frequency (ca 20-30%). As shown here, such variants cannot be induced at high frequency by irradiation of wild-type GH3 cells with ultraviolet light, indicating that the effect may be specific to treatment with alkylating agents. Furthermore, the DNA methylation inhibitor 5-azacytidine reverted an ethyl methanesulfonate-induced rPRL-deficient variant into rPRL-expressing cells at high frequency (ca 50%). The revertants were stable for at least 30-35 generations. These results support the hypothesis that the alkylating agent may promote the specific methylation of the rPRL gene or a gene regulating its activity, either one of which leads to inactivation of expression of the rPRL gene in GH3 cells. (Author abstract) (52 Refs)

42. CYTOCHEMICAL STUDY OF RNA IN CELLS OF ANTERIOR PITUITARY GLAND OF RATS WITH 7,12-DIMETHYLBENZ(A)ANTHRACENE (DMBA) INDUCED MAMMARY GLAND CARCINOMA.

Ganina KP, Iareshko AG
Inst. Problems Oncology, Kiev, USSR
Tsitol Genet; 16(1):3-6 1982

The functional activity of the anterior pituitary gland (APG) was studied in albino female rats subjected to iv administration of 7,12-dimethylbenz(a)anthracene (DMBA: 2 mg/day). Animals were sacrificed on days 10 and 40 after the termination of DMBA administration, and after the appearance of first palpable tumors of the mammary glands. Cytomorphological examination of the APG showed enhanced vascularization, progressive increase of the number of basophilic cells, and significant decrease of the number of acidophilic cells. The RNA content in the cytoplasm of basophilic cells showed decrease (from 1.51 units in controls, to 1.40 on day 10, 1.47 on day 40, and and 1.33 in tumor-bearing animals). RNA content in the nucleoli of basophilic cells was 1.01, 0.78, 0.87, and 0.76 units, respectively. Development of mammary gland tumors was associated with increase of RNA content in the cytoplasm and nucleoli of acidophilic cells. (13 Refs) (In RUS)

43. PROTON-TRANSLOCATING MG2+-DEPENDENT ATPASE ACTIVITY IN INSULIN-SECRETORY GRANULES.

Hutton JC, Peshavaria M
Dept. Clinical Biochemistry, Univ. Cambridge, New Addenbrooke's Hosp., Hills Road, Cambridge CB2 2QR, England
Biochem J; 204(1):161-170 1982

Insulin-secretory granules isolated from a pancreatic islet-cell tumor by centrifugation on Percoll density gradients exhibited a membrane-associated MG++-dependent ATPase activity. In granule suspensions incubated in iso-osmotic media, activity was increased two to three-fold by carbonyl cyanide p-trifluoromethoxyphenylhydrazone, the combination of valinomycin, nigericin and K2SO4 or by the addition of a detergent. Permeant anions also increased Mg++-dependent ATPase activity under iso-osmotic conditions when combined with K+ and nigericin, or NH4+. It was deduced that a major component of the activity was coupled to the translocation of protons into the granule interior. The granule membrane appeared poorly permeable to H+, K+, NH4+ and SO4-- but permeable, in increasing order, to phosphate or acetate, Cl-, I- and SCN-. Like the proton-translocating ATPase of mammalian mitochondria the granule enzyme when membrane-bound was inhibited by up to 85% by tributyltin or NN'-dicyclohexylcarbodi-imide and was solubilized in a tributyltin-insensitive form after extraction with dichloromethane. It was clearly not a mitochondrial contaminant as evidence by the distribution of marker proteins on density gradients. Unlike mitochondrial activity it was insensitive to oligomycin, efrapeptin, atractyloside, azide and oxyanions. Its properties, however, were indistinguishable from those of the proton-translocating ATPase found in the chromaffin granules of the adrenal medulla. Moreover, insulin granules and chromaffin granules exhibited similar levels of activity. This indicated that in spite of the differences in their internal composition, granules from tissue involved in polypeptide and amine hormone secretion possess catalytic components in common. Only a minor role for the ATPase in amine transport in insulin granules was apparent. Rather, its presence here may relate to the process of secretory vesicle morphogenesis or to the exocytotic mechanism. (Author abstract) (42 Refs)

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF PITUITARY ADENOMA.

Chen XR, Shen TZ, Chen GB, Tang SS
Hua Shan Hosp., 12 Wulumugi Zhong Road, Shanghai 200040, People's Republic of China
Comput Radiol; 6(3):125-135 1982

Computed tomographic (CT) findings in 85 patients with pituitary adenomas are described. Forty-four cases were operated upon and histological diagnoses of chromophobic adenoma (20), eosinophilic and chromophobic mixed adenoma (13), and eosinophilic adenoma (11) made. The remaining 41 cases were diagnosed based on typical endocrinological changes and clinical manifestations. Another 39 patients in whom tumors involved the sellar and parasellar region and were verified by operation and histology were also analyzed for comparison. All patients but two received 100 ml of 60% glucamine diatrizoate iv for enhancement before a second set of scans were taken. Without enhancement, the suprasellar cistern was obliterated in 10 cases and a filling defect was demonstrated in the

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anterior portion of the suprasellar cistern in 60 cases. In the 79 cases which revealed an abnormal suprasellar cistern, the density of the tumor region was homogeneous in 53 cases and nonhomogeneous in the remaining 26. Enhancement increased apparent density of the lesions, including those in two patients whose unenhanced study was negative. Enhancement also demonstrated the contour of the lesion and the cystic area more clearly. CT appearances of craniopharyngiomas, meningiomas, gliomas, and other lesions are also described. When the intrasellar pituitary adenoma, especially microadenoma, did not involve the suprasellar cistern, it was very difficult to detect by the CT scanner used in these studies. (13 Refs)

2. COMPUTED TOMOGRAPHY IN EVALUATION OF THE PARANASAL SINUSES.

Bilaniuk LT, Zimmerman RA
Dept. Radiology, Hosp. Univ. Pennsylvania Sch. Medicine, 3400 Spruce St., Philadelphia, PA, 19104
Radiol Clin North Am; 20(1):51-66 1982

Computed tomography (CT) in the evaluation of the paranasal sinuses (PNS), approach to the lesions, technique, and types of PNS lesions, are discussed. Both CT and pluridirectional tomography (PT) are excellent techniques for detecting erosions of bone. PT reveals not only bony changes but also soft tissue masses in areas that are normally seen in profile because of the contrast between air and soft tissues. CT examination of PNS consists of a series of contiguous sections obtained in the axial and coronal planes. Rotation of patient's head must be avoided so that a section includes the same portion of each sinus, permitting comparison between two sides. CT is useful in a wide spectrum of PNS lesions; congenital or developmental abnormalities, trauma, inflammation, and neoplasms. Malignant tumors of PNS usually produce both a mass and bony destruction. While some inflammations produce both bony destruction and a mass, on occasion malignant tumors may mimic inflammation by producing sinus opacification without bony destruction. Lesions that expand or encroach upon the PNS by means of pressure erosion include mucoceles, cysts, polyps, neurinomas, neurofibromas, epidermoids and dermoids, aneurysms, pituitary adenomas, fibro-osseous lesions, and chordomas. Some of these may expand the PNS to such a degree and produce such thinning of bony walls that the expansile quality may be missed on conventional radiographic studies and a false diagnosis of destructive malignant tumor or inflammatory lesion is made. With CT the thin bony margin and the sharp interface with adjacent tissue is correctly demonstrated. CT findings should be interpreted in the framework of the clinical picture. (30 Refs)

3. DIAGNOSIS OF PITUITARY TUMORS BY HORMONE ASSAYS AND COMPUTERIZED TOMOGRAPHY.

Valenta LJ, Sostrin RD, Eisenberg H, Tamkin JA, Elias AN
Diabetes and Endocrine Clinic of North County, 2131 El Camino Real, Oceanside, CA, 92054
Am J Med; 72(6):861-873 1982

One hundred and seventy patients with endocrine abnormalities, 29 males and 141 females, were studied by computerized tomography (CT) scanning of the pituitary and by pituitary hormone assays including basal and stimulated hormone concentrations in the blood. Pituitary macroadenoma was observed in 40 of the 170 patients, microadenoma in 49, primary empty sella in 46, secondary empty sella in 25, including 20 of the 40 patients with macroadenoma after surgical removal or radiation therapy of the tumor. Suprasellar tumor was present in four patients. In 23 women with menstrual abnormalities and 3 men with impotence and hyperprolactinemia, the results of CT scanning were normal. Of the 40 patients with macroadenoma, 24 presented with a hyperfunctioning syndrome (acromegaly or hyperprolactinemia). Among the 49 patients with microadenomas, 46 had the amenorrhea-galactorrhea syndrome, one male presented with acromegaly and one with Cushing's disease, and one female also had Cushing's disease. Primary empty sella was associated with the amenorrhea-galactorrhea syndrome in females and impotence in males. Only four female patients demonstrating an empty sella were asymptomatic. Distinctive biochemical findings were identified in certain groups of patients with different pituitary pathologic features. CT scanning was found very useful in the assessment of the size of the tumor, its suprasellar or parasellar extension and response to therapy, and in differential diagnosis of tumor and empty sella. Disappointing results were obtained in patients with endocrine abnormalities and normal results of CT scanning, and in patients following surgical treatment for a pituitary tumor, when the identification of recurrent tumor was impossible for a single examination. It is concluded that CT scanning is the most advanced technique in the diagnosis of anatomic pituitary abnormalities, and it should replace the traditional invasive diagnostic procedures. (Author abstract) (21 Refs)

4. EFFECT OF TAMOXIFEN ADMINISTRATION ON PROLACTIN RELEASE BY INVASIVE PROLACTIN-SECRETING PITUITARY ADENOMAS.

Lamberts SW, Verleun T, Oosterom R

Dept. Medicine III, Univ. Hosp. Dijkzigt, 40, Dr. Molewaterplein, 3015 GD Rotterdam, The Netherlands

Neuroendocrinology; 34(5):339-342 1982

Bromocriptine treatment of patients with invasive prolactin (PRL)-secreting pituitary adenomas does not invariably result in normalization of the plasma PRL levels. We previously showed that the antiestrogenic drug tamoxifen inhibited hormone release from transplantable PRL-secreting pituitary tumors in rats. In eight patients with invasive PRL-secreting pituitary adenomas with extrasellar extension, the effect of the administration of tamoxifen was investigated on the plasma PRL concentration and on the bromocriptine-mediated inhibition of PRL release. Treatment for 5 days with tamoxifen (20 mg/day) suppressed plasma PRL levels as measured in 5 samples over the day significantly by 20 +-3% (means +- SEM; p less than 0.01). During tamoxifen administration the inhibition of PRL secretion by 2.5 mg bromocriptine was further suppressed by 36 +-7%, in comparison with the plasma PRL levels after bromocriptine alone p less than 0.01). Tamoxifen administration suppressed PRL release in patients with giant invasive PRL-secreting pituitary adenomas, and it had a slight but significant additive or potentiating effect on the bromocriptine-mediated inhibition of PRL secretion. However, despite the simultaneous administration of bromocriptine and tamoxifen, normalization of the circulating PRL levels was not reached in this type of patient. (Author abstract) (12 Refs)

5. MENSTRUAL FUNCTION AND SERUM PROLACTIN LEVELS AFTER LONG-TERM BROMOCRIPTINE TREATMENT OF HYPERPROLACTINAEMIC AMENORRHOEA.

Bergh T, Nillius SJ, Wide L
Dept. Obstetrics and Gynecology, Clinical Chemistry, Univ. Hosp., S-750 14 Uppsala 14, Sweden
Clin Endocrinol (Oxf); 16(6):587-593 1982

Long-term bromocriptine treatment was discontinued in 37 women with hyperprolactinemic amenorrhea. After cessation of therapy 30 of the 37 women became hyperprolactinemic again with amenorrhea or anovulatory bleeding. Seven of the women continued to have regular ovulatory menstruation but only three were normoprolactinemic 3 months after stopping treatment. Two of the seven women had evidence of pituitary tumor regression. After the discontinuation they had nearly normal prolactin levels but during 2 years of follow up the serum prolactin levels slowly increased. In the 27 women with pre-treatment prolactin levels below 100 ug/l there was no difference between the prolactin levels before starting and 1 month after stopping treatment, while the women with pre-treatment prolactin levels above 100 ug/l had lower levels after therapy. Bromocriptine treatment seldom results in permanent cure of hyperprolactinemia amenorrhea. (Author abstract) (10 Refs)

6. DISCORDANT CORTISOL RESPONSE TO EXOGENOUS ACTH AND INSULIN-INDUCED HYPOGLYCEMIA IN PATIENTS WITH PITUITARY DISEASE.

Borst GC, Michenfelder HJ, O'Brian JT
Endocrinology Branch, Natl. Naval Medical Center, Bethesda, MD, 20814
N Engl J Med; 306(24):1462-1464 1982

It has been suggested that the iv response to ACTH accurately predicts the integrity of the hypothalamic-pituitary-adrenocortical (HPA) axis without causing the side effects due to insulin-induced hypoglycemia. However, the short ACTH stimulation test in four patients with pituitary tumors failed to reveal abnormalities of the HPA axis that were demonstrated by the insulin-tolerance test. (11 Refs)

7. PITUITARY ADENOMAS.

Sheline GE
Div. Radiation Oncology, Univ. California, San Francisco, CA
Oncologic 12: 197 pp., 1981.

Pituitary adenomas are discussed and in the three sections the following are included a 'self-instructional text' which features answers and comments to specific questions asked in the text, a 'study guide' with spaces for the reader to write responses, and a 'post-test' unit for the reader to send in for grading and receive continuing education credits. The main presentation consists of many figures, graphs, radiographs, and photographs related to the areas treated: acromegaly, Cushing's disease, prolactin-secreting tumors, tumors due to mass effects, and craniopharyngiomas. Some areas reviewed for acromegaly include clinical presentation, work-up procedures, radiographic presentation, anatomy and physiology, incidence and etiology, staging, and various forms of treatment. Some areas treated with regard to prolactin-secreting tumors includes surgical treatment, 'empty sella', and radiation therapy. The self-instructional and self-evaluation portions of the book are designed to help the reader to examine his decision-making ability as regards pituitary tumors. (105 Refs)

8. SURGICAL MANAGEMENT OF PINEAL AREA TUMORS IN EARLY CHILDHOOD.

Demakas JJ, Sonntag VK, Kaplan AM, Kelley JJ, Waggener JD
(c/o Sonntag) 222 West Thomas Road, Phoenix, AZ, 85013
Surg Neurol; 17(6):435-440 1982

Three cases of tumors of the pineal area in young children are presented. Surgical intervention is advocated because of the greater than 50% chance of the tumor's being benign in this age group and the greater risk from radiation to the developing brain. (Author abstract) (29 Refs)

9. PATHOLOGICAL AND CLINICAL BASIS OF THE INDICATIONS FOR TREATMENT OF CRANIOPHARYNGIOMAS.

Kobayashi T, Kageyama N, Yoshida J, Shibuya N, Yonezawa T
Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, Nagoya 466, Japan
Neurol Med Chir (Tokyo); 21(1):39-47 1981

Pathological and clinical studies were performed concerning the indications of operative treatment for craniopharyngiomas with seven autopsied brains and 15 cases which had been treated by extensive removal of the tumor. From the present study, it could be concluded that the total removal of the tumor was not always possible without potential neuroendocrinological deficits. The pathological basis is that the tumor cells invaded adjacent brain structures as finger-shaped or island-like protrusions without significant glial clevage and with close approximation to the neurons of the micron order in some cases, while in the other cases, a thicker layer of gliosis included Rosenthal fibers and fibrillary astrocytes existed between the tumor and neuronal structures. From the clinical study, the risk factors in the indication of extensive removal of craniopharyngioma could be correlated with the prognosis. These factors are the size and the location of the tumor, the existence of diabetes insipidus and psychiatric signs, and more significantly an irregular defect in the floor of the third ventricle. (Author abstract) (23 Refs)

10. INTRACAPSULAR IRRADIATION THERAPY OF CRANIOPHARYNGIOMAS WITH RADIOACTIVE GOLD: INDICATION AND FOLLOW-UP RESULTS.

Kodama T, Matsukado Y, Uemura S
Dept. Neurosurgery, Kumamoto Univ. Medical Sch., Kumamoto 860, Japan
Neurol Med Chir (Tokyo); 21(1):49-58 1981

Sixteen cases out of 27 patients with craniopharyngiomas were arbitrarily subjected to combined treatment of simple surgical evacuation and intracapsular irradiation with 198-Au. Follow-up studies were performed on 15 cases and they ranged from 6 mo to 11 yr. One patient was omitted from the study because of short postoperative period. Immediate postoperative morbidity and the endocrine functions at the end of the follow-up study were compared with those of the patients who underwent extensive surgical resection of the tumors. Intracapsular irradiation with 198-Au was found to have satisfactory effects in the treatment of cystic craniopharyngioma, especially in recurrent cases of initially solid tumors, with respect to the preservation of the endocrine functions and the daily activity of the patients. The immediate postoperative hazards in the patients' care were also much less and they were found to be easily manageable. The patients, who had been followed up for over 5 yr, maintained an occupational IQ score in the normal range and the patients under school age were all able to continue their school lives. One of the female patients, who had been married after the treatment, could have two children without any specific replacement therapy, and another patient in childhood who had shown physical retardation due to HGH deficiency, showed favorable results with crescormon administration in comparison with cases of extensive resection. Although the dosimetric value of 198-Au should be varied according to the size and thickness of the capsule, it was found that 15 to 30 mCi of 198-Au was the appropriate dose for treatment. (Author abstract) (10 Refs)

THYROID TUMORS

11. FINE NEEDLE ASPIRATION AND LESIONS OF THE THYROID.

Block MA
Dept. Surgery, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037
Int Adv Surg Oncol; 5:1-27 1982

Needle biopsy techniques, focusing on fine needle aspiration biopsy (FNAB), are reviewed. Three major needle biopsy diagnostic techniques are used for thyroid nodules: FNAB, large needle aspiration biopsy, and large cutting needle biopsy. In general, cytologic and histologic studies of needle biopsy can be categorized into four groups: benign, malignant, indeterminate, and inadequate for diagnosis. Needle biopsy specimens of papillary carcinoma may contain follicular, papillary, or a combination of patterns provided as single cells, groups of cells, monolayered sheets, or as papillary fragments. Microscopic patterns and features of particular importance are presented. Follicular carcinoma is recognized on the basis of cytologic features of carcinoma, but the spectrum ranges from minimal atypia to pronounced nucler abnormalities. Medullary carcinoma provides specimens with a variety of cellular morphology and with variable degrees of pleomorphism. Anaplastic carcinoma appears as severe pleomorphism in cells, with great variations in the size and shapes of cells and nuclei. Problem situations in the diagnosis of thyroid nodules by needle aspiration and causes of false negative reports are presented. The critical assessment of the value of needle biopsy of the thyroid relates primarily to the occurrence of false negative and false positive reports. The impact of needle biopsy in the management of thyroid nodules and carcinoma has been predominantly manifested in the selection of patients with thyroid nodules for operation. Recorded experience with needle biopsy of thyroid nodules is presented. (40 Refs)

12. FINE NEEDLE ASPIRATION OF THYROID COLD NODULES.

Gaham N, Rocmans P, Ketelbant-Balasse P, Verelst J, Mockel J, Glinoer D
Service de Medecine Interne, Hopital Universitaire Saint-Pierre 322, rue Haute, B-1000 Brussels, Belgium
Ann Endocrinol (Paris); 42(6):543-544 1981

Fine needle aspiration (FNA) was performed in 160 patients with thyroid cold nodules. In 144 (90%) patients adequate cytological material was aspirated for examination. In 128/144 (89%) of the cases, a benign lesion was diagnosed from the aspirate. In 16/144 (11%), there was an indication of a cancerous lesion. A total of 51 patients underwent surgery,and benign lesions were found in 39/41 patients with benign cytology, and malignant lesions were found in 5/10 patients with suspect cytology. In 20-30% of the patients antithyroid antibodies were found. In a retrospective review of 100 patients who underwent surgery for thyroid cold nodules, 92 had benign lesions, and 8 had thyroid cancer. FNA of cold nodules permitted significant improvement in the clinical diagnosis of nodules when results from the retrospective and prospective studies were compared. Cytological false negatives were rare, but caution is recommended in the follow-up of cases with benign cytology because two false-negatives did occur. (no Refs) (In FRE)

13. FINE-NEEDLE ASPIRATION VERSUS DRILL-NEEDLE BIOPSY OF THYROID NODULES: A CONTROLLED CLINICAL TRIAL.

Boey J, Hsu C, Wong J, Ong GB
(c/o Ong), Queen Mary Hosp., Hong Kong, Hong Kong
Surgery; 91(6):611-615 1982

Percutaneous needle biopsy by two different methods was evaluated in a prospective controlled study of 167 consecutive patients with dominant thyroid nodules. Fine-needle aspiration was superior to high-speed drill-needle biopsy because of its high diagnostic yield (93.9%). When a sample sufficient for diagnosis was obtained, the accuracy rate for both methods was comparable. Diagnostic errors were due to inadequate samples, difficulties in interpreting hypercellular adenomas, and geographic sampling problems. In the detection of thyroid cancers, neither technique alone appears completely adequate because of occasional false negative errors. The selection of patients for operation should depend on clinical parameters as well as the findings of fine-needle aspiration of thyroid nodules. (Author abstract) (18 Refs)

14. THYROID NODULES AFTER HIGH-DOSE EXTERNAL RADIOTHERAPY. FINE-NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS AND MANAGEMENT.

Pretorius HT, Katikineni M, Kinsella TJ, Barsky SH, Brennan MF, Chu EW, Robbins J
(c/o Robbins) Clinical Endocrinology Branch, NIH, Bethesda, MD, 20205
JAMA; 247(23):3217-3220 1982

From 1974 to 1980, we studied six patients, five treated for Hodgkin's disease and one for a hemangioma, in whom thyroid nodules developed after high-dose (2,500 to 4,000 rad) thyroid radiation. Fine-needle aspiration cytology of the thyroid in five cases showed moderate to severe cellular atypia in four (3 of whom had elevated serum thyrotropin levels) and mild atypia in one (who was overtly hypothyroid). In the four with marked atypia, surgical pathology disclosed Hashimoto's thyroiditis in one, diffuse hyperplasia and epithelial atypia in two, and a sclerosing papillary carcinoma in one. Among five patients who had total thyroidectomy, three had carcinoma (microscopic papillary, papillary- follicular, or sclerosing papillary) in addition to one or more follicular adenomas or colloid nodules. Thyroid nodules and neoplasia may be more common than previously appreciated in patients exposed to high-dose radiation. (Author abstract) (20 Refs)

15. A CLINICO-PATHOLOGICAL STUDY OF 100 PATIENTS WITH SOLITARY 'COLD' THYROID NODULES.

Cutfield RG, Croxson MS
(c/o Croxson) Endocrinology Dept., Auckland Hosp., Auckland, New Zealand
NZ Med J; 93(684):331-333 1981

Clinical features were analyzed retrospectively for a population 89 women and 11 men (av 38 yr old; range 8-64 yr), who had undergone surgical excision of a 'cold' thyroid nodule. Adenoma was found in 44 patients, cyst in 14, colloid nodule in 25, and carcinoma in 17. Statistical analysis demonstrated only that patients less than 40 yr old were more likely to have carcinoma or neoplasm than older patients. No other significant relationship between clinical features and pathological diagnosis was found. The frequency of carcinoma was not different in males and females. Three of the 17 patients with a family history of goiter, 2/14 with a small nodule, 2/15 with a palpable nodule, and 1 patient with a painful nodule had carcinoma. Carcinomas were found in 4/31 patients with a cool nodule and 4/23 with a suspected abnormality elsewhere in the scan. Four/17 patients with carcinoma had significant amounts of hemorrhagic or cystic fluid. The patient with overt multinodular goiter is readily detected by a combination of careful neck palpation and thyroid scanning. Hashimoto's thyroiditis can be excluded by the test for serum antimicrosomal antibodies. Past history of neck irradiation, evidence of clinical carcinoma, vocal cord paralysis, or regional node enlargement are definite indications for surgery. The risk of malignancy is halved by the presence of a warm nodule and insignificant in patients with hot nodules. Follicular carcinoma is difficult to diagnose preoperatively. (15 Refs)

16. ANATOMOPATHOLOGICAL DATA ON CANCER OF THE THYROID IN WALLONIE (BELGIUM).

Flevez M, Flevez-Charon C, Damoiseau JY
Institut de Morphologie Pathologique, 41, allee des Templiers, B-6270 Loverval, Belgium
Bull Cancer (Paris); 69(2):164-166 1982

Pathological findings for thyroid specimens obtained from 3,977 patients (572 males, 3,415 females; mean age 44.1 yr) operated on for thyroid disorders (3,365 cases of goiter, 60 thyroiditis, 203 adenomas, 180 hyperthyroidism, and 169 cancers) are reported. Of the 169 cancer patients (107 males, 126 females; 9-85 yr old), 48.4% were between 30 and 60 yr old; the mean age of the patients was 49.3 yr. Histologically the thyroid tumors were papillary (34.9%), follicular (40.2%), medullary (5.9%), or anaplastic (18.1%). The results indicated that thyroid cancer is relatively rare among thyroid diseases, decreases in frequency in older patients, and shows a constant frequency in males. Extemporaneous examination of 697 patients revealed 37 cancers; examinations produced 10 diagnostic errors, including 3 false positives. (14 Refs) (In FRE)

17. UNUSUAL CYTOPLASMIC INCLUSION BODIES IN MEDULLARY CARCINOMA OF THE THYROID GLAND.

Kakudo K, Spurlock BO, Miyauchi A, Kuma K, Shimaoka K, Matsuzuka F
Dept. Pathology, Hyogo Coll. Medicine, 1-1 Mukagawa, Nishinomiya 663, Japan
Acta Pathol Jpn; 32(2):319-326 1982

Medullary carcinoma of the thyroid from a 43-year-old patient showed four types of unusual cytoplasmic inclusion bodies ultrastructurally. Type 1 inclusion is composed of rod and doughnut-shaped bodies aggregated in the cytoplasma and not enclosed by a limiting membrane. Typical neurosecretory granules are intermingled with the rod and doughnut-shaped bodies. The doughnut-shaped bodies often have an electron dense core which is similar to the neurosecretory granules. The rod-shaped bodies are bounded by trilaminar unit membrane and have a slightly electron dense matrix. A centriole is often found associated with this type of inclusion. Type 2 inclusion is composed of small secretory granules and clear vesicles. These inclusions can be found either with or without surrounding membrane. Type 3 inclusion is a large osmiophilic body, or secondary lysosome, in which some degenerated organelles are discernible. Type 4 inclusion is a fragmented nucleus with condensation and margination of the chromatin, so-called karyorrhexis. Routine hematoxylin and eosin sections did not show each type of inclusion but semithin sections stained with Paragon suggested four different types of inclusions. Type 3 and 4 inclusions represent forms of degeneration and cell death in the tumor cells and probably represent a remote effect of radiation. Type 1 inclusion is not commonly associated with cell death and may represent a unique organellar aberration in these tumor cells. Type 2 inclusion is simply an aggregation of secretory granules and clear vesicles. (Author abstract) (26 Refs)

18. FOLLICULAR CARCINOMA OF THE HUMAN THYROID GLAND: AN ULTRASTRUCTURAL STUDY WITH EMPHASIS ON SCANNING ELECTRON MICROSCOPY.

Johannessen JV, Sobrinho-Simoes M
Dept. Pathology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Diagn Histopathol; 5(2):113-127 1982

Combined transmission electron microscopy (TEM) and scanning electron microscopy (SEM) were used to study the size, shape, and number of microvilli and cilia in follicular carcinoma of the thyroid cells, and to relate endocrine function or degree of tumor differentiation to structural characteristics of tumor cells. Tumor tissue from nine patients (7 women, 2 men; 36-76 yr old) was examined. Indented nuclear membranes, clumps of heterochromatin, interchromatin granules, nucleoli, and complex nuclear bodies were more frequent in moderately differentiated tumors than in well-differentiated lesions. The findings were even more marked in anaplastic foci. The percentage of ciliated cells varied within each tumor and was greater in the follicles lined by planar or concave cells than in those lined by cells with a convex surface. SEM was inferior to TEM in revealing abortive follicles in thyroid tumors that had a solid growth pattern by light microscopy, but SEM did demonstrate marked morphological differences between well-differentiated and moderately differentiated follicular carcinomas. TEM and SEM techniques correlated morphology with behavior of tumors, but determining whether observed changes in follicular carcinomas were related to endocrine function or malignant potential was not possible. Interpretation of isolated ultrastructural findings is difficult, thus reducing the usefulness of ultrastructural methods in diagnosis. (37 Refs)

19. HETEROMULTINODULAR GOITERS: CLINICAL AND THERAPEUTIC STUDY.

Hubinois P, Mogenet M, Reynier J
Clinique Chirurgicale, Hopital Boucicaut, 78, rue de la Convention, F 75730 Paris, Cedex 15, France
Nouv Presse Med; 11(12):923-926 1982

Heteromultinodular goiters are frequent and the involutive forms require early surgical treatment for three reasons: these goiters are usually resistant to medical treatment; association with carcinoma is not uncommon (6.5% in this series); and late surgery is hazardous, as it leads to extensive tissue resection and often entails a risk of recurrence and lesions of the parathyroid glands. Post-operative hormonal treatment should be reserved for those patients who have had wide tissue resection (replacement therapy for life, monitored by TSH assays) or for young patients who require a 2-yr protective treatment. Prevention may perhaps be achieved by systematic 2-3 yr treatment of active homogenous hyperplasia in young subjects. Hyperplasia has a natural tendency to nodular involution, in most cases over several decades, but curiously, 30-35 yr old adults with large multi-nodular goiters are being operated upon as though these lesions had greater evolutive potential. This could be an argument in favor of post-operative protective therapy in these young patients. (Author abstract) (10 Refs) (In FRE)

20. ABLATION OF NONMALIGNANT THYROID REMNANTS WITH LOW DOSES OF RADIOACTIVE IODINE: CONCISE COMMUNICATION.

Ramacciotti C, Pretorius HT, Line BR, Goldman JM, Robbins J (c/o Robbins), NIH, Building 10, Room 8N315, Bethesda, MD, 20205
J Nucl Med; 23(6):483-489 1982

Ablation of nonmalignant thyroid tissue (present after thyroid carcinoma surgery) with I-131 is associated with decreased recurrence rates and probably increased survival. Low-dose therapy (30 mCi) has been controversial. We studied the effects of low-dose therapy in 20 patients. Complete ablation of thyroid tissue, using a 1-1.5-mCi test dose, occurred after a single 30-mCi dose in eight patients and in one of seven patients who were treated again with the same dose. In three of these patients, a minimally positive scan at 6 mo became negative without further therapy. These results compared favorably with those of a single 75-mCi dose. In 19 of the 20 patients, one or two doses of 30 mCi reduced thyroid iodine uptake to a level much less than that of normal nonthyroid neck tissues; ie, one that causes no significant interference with the diagnosis or therapy of malignant lesions. We conclude that the use of up to two 30-mCi doses at 6-mo intervals is a reasonable approach to ablation therapy, particularly in young subjects with well-differentiated thyroid cancer. Besides minimizing whole-body and gonadal irradiation exposure, the advantages are greater convenience and reduced expense with a dose that can be given to outpatients. The disadvantages are that about half of the patients will require more treatment, with attendant hypothyroid periods and delay in achieving ablation, and that any tumor in the thyroid remnant may be inadequately irradiated. A long-term, prospective study is needed to evaluate the importance of these factors. The persistence of a positive scan after two 30-mCi doses appears to be an indication for increasing the subsequent dose, as would the detection of I-131 uptake in tumor tissue at any stage. In older patients and in poorly differentiated thyroid cancer, high-dose therapy at the outset may be preferable. (28 Refs)

21. SIGNIFICANCE OF THYROGLOBULIN AS A TUMOR MARKER IN THE SERUM OF PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA: LONGITUDINAL AND CROSS-SECTIONAL STUDIES.

Schatz H, Grebe S, Maser E, Teuber J, Horn W, Schroder O, Schatz C
III. Med. Univ.-Klinik und Poliklinik, Rodthohol 6, D-6300 Giesser, W. Germany
Klin Wochenschr; 60(9):457-464 1982

For evaluating the clinical significance of thyroglobulin measurements for the follow-up of patients with differentiated thyroid carcinoma, thyroglobulin was determined radioimmunologically during the past 2 yr (up to 12x) in 40 patients after withdrawal of thyroid hormone. Thyroglobulin values were compared with whole-body scintigrams after radioiodine. Thyroglobulin antibodies, which may interfere in the radioimmunoassay for thyroglobulin, were also estimated by a radioimmunologic method. In the majority of cases, thyroglobulin levels corresponded to the scintigrams, however, the thyroglobulin level appeared to be a more precise index for changes in tumor tissue mass. In one patient the scintigram was negative, whereas considerable amounts of thyroglobulin were measured in the serum: x-ray tomography revealed a lung metastasis in this case. On the other hand, thyroglobulin was undetectable in the sera of patients who exhibited distinct metastases in the scintigram. Thyroglobulin can be regarded as a tumor marker in patients thyroidectomized for differentiated thyroid carcinoma. However, its determination can certainly not replace whole-body scintigraphy as postulated by several authors, although thyroglobulin measurement appears to be superior to scanning in some cases. A combined application of iodine scanning and thyroglobulin radioimmunoassay is thus advisable in the follow-up of patients with differentiated thyroid carcinoma. (Author abstract) (18 Refs) (In GER)

22. HETEROGENEITY OF PLASMA AND URINARY IMMUNOREACTIVE CALCITONIN IN PATIENTS WITH MEDULLARY CARCINOMA OF THE THYROID.

Morimoto S, Okada Y, Onishi T, Takai S, Miyauchi A, Lee S, Nishioka Y, Kumahara Y

Dept. Medicine and Geriatrics, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan

Endocrinol Jpn; 28(5):583-594 1981

Disappearance of the calcitonin (CT) forms from the blood after calcium infusion (CAI) and total thyroidectomy, and the relation of urinary and plasma CT were studied in two female patients (14 yr old, patient A; 65 yr old patient B) with medullary carcinoma of the thyroid. The two antisera (antiserum I and antiserum II) had similar binding affinities for (1-32)human CT (hCT) monomer. Antiserum I appeared to have a major antigenic site within residues 21-32 of hCT monomer and a minor antigenic site within residues 21-32 of hCT, while the antiserum II appeared to have a major antigenic site within residues 11-16 and a minor antigenic site within residues 17-20. In all samples, values for immunoreactive hCT concentration measured by immunoassay with antiserum I were 1.08-1.79x higher than those measured by immunoassay with antiserum II. Immediately after CAI, the serum calcium level increased from 9.0 to 10.8 mg/deciliter (dl) in patient A and from 9.2 to 11.2 mg/dl in patient B. The plasma hCT level increased to 10.6 and 9.6x the initial level in patient A, and to 11.9 and 12.0x the initial level in patient B, as estimated with antiserum I and II, respectively. Very high levels of immunoreactive CT levels were found in the urine of both patients. The elution patterns of the basal plasma samples of both patients on the Bio Gel P-30 column are compared. In both patients, all forms of CT increased immediately after CAI. The level of immunoreactive CT in urine samples also decreased in both patients after thyroidectomy. Results indicated that serum CT in various forms including the monomer may be converted to form IIIb in the kidney and excreted in that form. (43 Refs)

PARATHYROID TUMORS

23. PREOPERATIVE TECHNETIUM-99M IMAGING OF A SUBSTERNAL PARATHYROID ADENOMA.

Naunheim KS, Kaplan EL, Kirchner PT
(c/o Kaplan) Dept. Surgery, Univ. Chicago Hosp., Box 402, 950 East 59th St., Chicago, IL, 60637
J Nucl Med; 23(6):511-513 1982

Preoperative radionuclide imaging of parathyroid glands has been attempted using various nuclides with varying degrees of success. We present a case report of preoperative location of a mediastinal parathyroid adenoma with pertechnetate (Tc-99m) imaging. The literature on parathyroid imaging with technetium is reviewed. We conclude that pertechnetate may have been overlooked as a useful imaging agent for parathyroid adenomas, especially for tumors located away from the thyroid, and that further investigation is warranted. (Author abstract) (13 Refs)

24. SURGERY FOR PRIMARY HYPERPARATHYROIDISM: EXPERIENCE WITH 500 CONSECUTIVE CASES AND EVALUATION OF THE ROLE OF SURGERY IN THE ASYMPTOMATIC PATIENT.

Russell CF, Edis AJ
Dept. Surgery, Mayo Clinic and Mayo Foundation, Rochester, MN
Br J Surg; 69(5):244-247 1982

A group of 500 patients with a presumptive diagnosis of primary hyperparathyroidism (HPT) was operated upon at the Mayo Clinic between September 1974 and May 1980 using a standardized operative strategy. Clinical profiles, biochemical data, operative findings and pathological changes are reviewed. Of the 500 patients, 461 (92.2%) were cured after primary cervical exploration. One patient died during the postoperative period, 1 had a permanent unilateral vocal cord paralysis and 10 (2%) had protracted hypoparathyroidism. Owing to the continuing controversy regarding the appropriate therapeutic management of asymptomatic, uncomplicated and mild ('biochemical') primary HPT, we further evaluated this surgical experience by comparing the results of operation in two groups of patients: those with 'biochemical' HPT (serum calcium less than 11 mg/dl) and those with 'non-biochemical' HPT (symptomatic or complicated disease or serum calcium greater than 11 mg/dl). The cure rate in each patient group was greater than 90%. A statistically significant increase in the incidence of negative cervical exploration (4 normal parathyroid glands identified and biopsied) was noted in the 'biochemical' group. However, parathyroid disease was found at operation in 92% of these patients. We conclude that cervical exploration in all patients with primary HPT, including those with 'biochemical' disease only, is safe and that such an aggressive management policy is justified. (Author abstract) (8 Refs)

25. THERAPY OF HYPERCALCEMIA DUE TO PARATHYROID CARCINOMA WITH INTRAVENOUS DICHLOROMETHYLENE DIPHOSPHONATE.

Shane E, Jacobs TP, Siris ES, Steinberg SF, Stoddart K, Canfield RE, Bilezikian JP
(c/o Bilezikian) Dept. Medicine 8-405, Coll. Physicians and Surgeons, 630 West 168th St., New York, NY, 10032
Am J Med; 72(6):939-944 1982

Dichloromethyiene diphosphonate (Cl2MDP), a potent inhibitor of osteoclast-mediated bone resorption, lowers serum calcium in hypercalcemia associated with malignancies and with primary hyperparathyroidism, and reduces excess calcium mobilization from bone in multiple myeloma and in Paget's disease. We have evaluated the effectiveness of intravenously administered Cl2MDP in five patients with parathyroid carcinoma, a disorder characterized by severe hypercalcemia, very high parathyroid hormone (PTH) levels, and marked osteoclast-mediated bone resorption. All patients had biopsy-proved metastatic parathyroid carcinoma and hypercalcemia which persisted after multiple surgical procedures and other attempts at management. During a 3-day observation period, each patient continued to demonstrate stable or progressive hypercalcemia despite infusion with saline soln and furosemide. Cl2MDP was administered over 2 hr at 2.5 mg/kg on Day 1 and 5 mg/kg on Days 2 through 7. Response was noted in all five patients; there was a gradual decline in the av serum calcium by the 8th day. There were concomitant reductions in urinary calcium excretion, and in the urinary hydroxyproline excretion. Serum PTH levels remained markedly elevated. In three patients, all indices returned to pretreatment levels by 10 days after the last infusion. In two of these patients there was a response to retreatment with Cl2MDP with a fall in calcium from 16.9 +-0.5 mg/dl to 12.4 +-1.5 mg/dl. There was no response in one patient. No adverse reactions to Cl2MDP were observed. The decrease in serum calcium and concomitant declines in urinary calcium and hydroxyproline suggest that Cl2MDP can effectively inhibit the excessive bone resorption associated with parathyroid carcinoma. (18 Refs)

26. THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND HYPERTENSION IN PRIMARY HYPERPARATHYROIDISM.

Ganguly A, Weinberger MH, Passmore JM, Caras JA, Khairi RM, Grim CE, Edmonson J, Johnston CC
Clinical Building Room 447, Indiana Univ. Sch. Medicine, 1100 West Michigan St., Indianapolis, IN, 46223
Metabolism; 31(6):595-600 1982

The status of the renin-angiotensin-aldosterone (RAA) axis was examined by well-defined stimulatory and suppressive maneuvers in 11 patients with primary hyperparathyroidism (10 with parathyroid adenomas). Mean plasma aldosterone levels were normal, while the mean plasma renin activity in response to furosemide stimulation was subnormal. Plasma and urinary norepinephrine concentrations were within the normal range. These results demonstrate that hypertension may occur in patients with hyperparathyroidism by a variety of mechanisms. (49 Refs)

ADRENAL TUMORS

27. COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF PRIMARY ADRENAL NEOPLASMS (MEETING ABSTRACT)

Zelch MG, Geisinger MA, Risius BF, Chilcote WA, Borkowski GP
No affiliation given
Eighty-second Annual Meeting of the American Roentgen Ray Society, May 10-14, 1982, New Orleans, Louisiana The American Roentgen Ray Society; :A231 1982

A five-year review of all primary adrenal pathology diagnosed at our institution was conducted. In over 100 patients, a definitive diagnosis of a primary adrenal neoplasm was established by surgery, biopsy, or compelling clinical evidence. These included pheochromocytomas, neuroblastomas, cortical adenomas and carcinomas, as well as the more uncommon adrenal neoplasms, such as myelolipomas. Since a CT had been performed on each of these patients, correlation of the pathology with CT (computed tomography) findings was possible. Both the typical presentation and characteristics of the various adrenal gland neoplasms as well as our accuracy in diagnosing them will be presented. (no Refs)

28. CEREBRAL INFARCTION AND DISSEMINATED INTRAVASCULAR COAGULATION WITH PHEOCHROMOCYTOMA.

Hill JB, Schwartzman RJ
(c/o Schwartzman) Div. Neurology, Dept. Medicine, Univ. Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX, 78284
Arch Neurol; 38(6):395 1981

The case of a 54-yr-old woman with disseminated intravascular coagulation (DIC), cerebral infarction, and hemorrhage secondary to malignant pheochromocytoma is reported. Incidence of DIC and nonbacterial thrombotic endocarditis and the roles of release of thromboplastin and endogenous catecholamines from neoplastic tissue and platelet aggregation in vasospasm, thrombosis, and death are discussed. (16 Refs)

29. A CASE OF VIP AND SOMATOSTATIN-SECRETING PHEOCHROMOCYTOMA.

Faurel JP, Bernard P, Saigot T, Bousquet O, Sarrazin A
Clinique des Maladies de l'Appareil Digestif, Hopital de la Salpetriere, 47, boulevard de l'Hopital, F 75651 Paris Cedex 13, France
Nouv Presse Med; 11(19):1483-1485 1982

A man with watery diarrhea was found to have adrenal tumor. Pre-operative examinations located the tumor in the right adrenal gland and revealed that it secreted an excess of vasoactive intestinal peptide (VIP). All symptoms disappeared after excision of the pheochromocytoma; they have not recurred after a 3 years' follow-up period. Histological examination of the tumor confirmed that it was the site of a triple hormonal secretion (VIP somatostatin and catecholamines). (Author abstract) (19 Refs) (In FRE)

30. FAMILIAL CONCURRENCE OF CAROTID BODY TUMOR AND PHEOCHROMOCYTOMA.

Pritchett JW
1806 E. Lane Ave., Phoenix, AZ, 85020
Cancer; 49(12):2578-2579 1982

Carotid body tumors and pheochromocytomas originate in paraganglionic tissue. Two cases of concurrent carotid body tumor and pheochromocytoma occurred in a single family. This familial pattern has not been previously described. (Author abstract) (8 Refs)

31. PHEOCHROMOCYTOMA IN MULTIPLE ENDOCRINE NEOPLASIA, TYPE 2; AN EXAMPLE OF THE TWO-HIT THEORY OF NEOPLASIA (MEETING ABSTRACT)

Cerny JC, Jackson CE

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Three kindred with pheochromocytoma and medullary carcinoma of the thyroid as dominantly inherited patterns typical of multiple endocrine neoplasia type 2 were studied. Patients underwent bilateral total adrenalectomy with the finding that the pheochromocytomas were a) bilateral, b) multifocal and c) associated with distinct medullary hyperplasia and reduction in the normal cortical-medullary ratio, features not usually seen in sporadic pheochromocytoma. These findings are exemplified in a recent case of a 34 year old female who previously had bilateral thyroidectomy for medullary carcinoma of the thyroid and whose mother had undergone thyroidectomy, parathyroidectomy and bilateral adrenalectomy. Diagnosis of pheochromocytoma was made by CT (computed tomographic) scan and guanidine scan even though catecholamine studies were equivocal. Bilateral adrenalectomy was performed with the finding of multiple, bilateral pheochromocytoma and adrenal medullary hyperplasia. As in hereditary medullary carcinoma of the thyroid, the pathology findings in pheochromocytoma MEN 2 are consistent with Knudson's two mutational event theory of the initiation of neoplasia, with adrenal medullary hyperplasia representing the manifestation of the first or genetic mutational event and present uniformly in the hereditary cases. (no Refs)

32. DEFECTIVE 11 BETA HYDROXYLATION IN PATIENTS WITH CONGENITAL ADRENAL HYPERPLASIA DUE TO 21 HYDROXYLASE DEFICIENCY.

Kolanowski J, Crabbe J
Endocrine Unit, Univ. Louvain (UCL 5530), B-1200 Brussels, Belgium
Ann Endocrinol (Paris); 42(6):537-538 1981

The 11-beta-hydroxylation step was assessed in seven patients with congenital adrenal hyperplasia (CAH) due to partial block of 21-hydroxylation, by means of simultaneous measurements of plasma 11-deoxycortisol (S) levels, 17-hydroxyprogesterone (17-OH-P), cortisol (F), and corticosterone (B) in baseline conditions as well as during corticotropin (ACTH) or metyraprone (MP) administration. Baseline plasma steroid levels (nanomole/liter) were 221 +-43 for F, 43.6 +-9.1 for S, 410 +-85 for 17-OH-P, and 22.7 +-7.3 for B. With reference to normal values, a 50 to 100-fold increase in plasma 17-OH-P existed with plasma F reduced to half of normal values, confirming the partial block of 21-hydroxylation. Plasma S was more than one order of magnitude higher than in normal subjects, indicating the existence of a defect in 11-beta-hydroxylase. Upon infusion of ACTH (250 ug tetracosapeptide iv over 8 hr), plasma F increased to 468 +-58 nanoM (nM), while plasma S increased to 102 +-39 nM. Following MP administration to three patients, plasma S did not exceed 221 +-30 nM, thus confirming that the activity of 21-hydrolase was reduced. Additional evidence for partial insufficiency of 21-hydroxylation was provided by the fact that plasma B reached only 46 +-13 nM upon ACTH infusion vs 170 +-17 nM in normal subjects. The rise in plasma 17-OH-P was considerably more marked in patients with CAH. (4 Refs)

33. ROUTINE ASSAY OF CATECHOLAMINES BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY WITH FLUORIMETRIC DETECTION.

Clough G
Biochemistry Dept., General Hosp., Harrogate HG2 7ND, England
Anal Proc; 19(4):183-186 1982

The assay of urinary catecholamines is useful in the investigation of patients with suspected neuroblastoma, neuroganglioma, or pheochromocytoma. An HPLC procedure for such analyses, suitable for routine handling of many samples and sensitive at the nanogram level, is described. Tumors of neurological origin, particularly neuroblastomas, do not produce vanillylmandelic acids at the levels detectable by conventional means. HPLC analysis enables the quantification of dopamine excretion in such patients, and based on this data the diagnosis can be established. (4 Refs)

34. THE HEMODYNAMIC RELEVANCE OF FREE AND CONJUGATED DOPAMINE IN PHEOCHROMOCYTOMA.

Kuchel O, Buu NT, Bourque M, Hamet P, Larochelle P
Clinical Res. Inst., 110 Pine Ave. West, Montreal, Quebec H2W 1R7, Canada
J Clin Endocrinol Metab; 54(6):1268-1270 1982

Two patients with adrenomedullary hypersecretion (confirmed pheochromocytoma and adrenomedullary hyperplasia) presented 15 spontaneous crisis associated with hypertension or hypotension with or without tachycardia. Correlation coefficients calculated between extreme values of pulse rates and of systolic and diastolic blood pressures on the one hand and plasma free and conjugated norepinephrine, epinephrine, and dopamine (DA) sampled at the height of the crisis on the other, showed no relationships between free or conjugated norepinephrine or epinephrine and blood pressure or pulse rate. However, plasma conjugated DA was negatively correlated with systolic blood pressures (p less than 0.02) and diastolic blood pressures (p less than 0.03) and free plasma DA was negatively correlated with pulse rates (p less than 0.001). These data suggest that the extremely high circulating level of conjugated DA in pheochromocytoma may, in the presence of high circulating conjugated norepinephrine and possibly high alpha-adrenergic receptor occupancy, decrease blood pressure by its predominant action on dopaminergic receptors while elevated free DA may decrease the tendency to tachycardia, possibly by lowering the venous return. (Author abstract) (12 Refs)

35. EVIDENCE FOR THE ROLE OF ANDROGENS IN THE FEEDBACK CONTROL OF GONADOTROPHIN SECRETION IN THE HUMAN FEMALE.

Gray P, Potgieter GM, Slabber CF, Veldsman JJ
Dept. Chemical Pathology, Univ. Orange Free State, Bloemfontein, South Africa
S Afr Med J; 61(22):837-838 1982

The effect of androgens on the luteinizing hormone (LH) response to LH-releasing hormone (LH-RH) is fairly well documented. However, the evidence concerning the effect on follicle-stimulating hormone (FSH) is less convincing and clear-cut. We administered LH-RH to a patient with an androgen-producing adrenal tumor both before and after removal of the tumor. Before operation, testosterone levels were elevated and estradiol levels reduced. There was no response of either LH or FSH levels to LH-RH on two separate occasions. Postoperatively LH-FSH values rose sharply, to 404% and 170% above basal levels respectively. The data suggest that androgens do play a role in the feedback control of both LH and FSH secretion. (Author abstract) (11 Refs)

PANCREAS TUMORS

36. DIAGNOSTIC PROBLEMS OF INSULINOMA.

Bai Y, Xu XH, Jin ZM, Liu W, Liu JH, Chi ZS
Endocrinology Dept., Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Chin Med J [Engl]; 95(3):181-185 1982

The clinical characteristics of insulinoma in 61 patients (52 males and 9 females) are described and compared with the symptomatology in pancreatic islet cell hyperplasia (PICH) in 3 patients (2 males and 1 female). Of the 61 cases, 57 were monoadenoma and 4 polyadenoma. Age of insulinoma onset ranged from 13-57 yr. Insulinoma diagnosis was confirmed on first visit in 10 cases, within 0.5 yr in 25, in 0.5-2 yr in 11, and in 2-6 yr in 11. the patients were classifiable into three groups based on symptoms: hypoglycemic coma (17 cases, including 1 PICH case); epileptic attack (37 cases, including 2 PICH cases); and other organic neuropsychiatric abnormalities (10 cases). Of the 61 cases, 26 were misdiagnosed, 13 as psychoneuroses, 9 as psychoses, and 1 each as olivopontocerebellar atrophy, myasthenia gravis, autonomic dysfunction, and Meniere's syndrome. Onset of attacks was closely related to meals, generally occurring before meal time or just post-feeding. Most attacks were relievable by feeding or iv glucose injection. Due to the close resemblance of insulinoma to neuropsychiatric disorders, differential diagnosis is difficult and may be delayed for years. Careful inquiry into past history (hypoglycemic attacks), fasting blood glucose determination, and time of attack occurrence may aid in the early diagnosis of this tumor. (13 Refs)

37. CONCOMITANT NEOPLASIA IN PANCREATIC CANCER.

Hartveit F, Maehle BO
Dept. Pathology, 5016 Haukeland Hosp., Bergen, Norway
Cancer; 49(11):2410-2413 1982

An association is reported between endocrine tumors and adenocarcinoma of the exocrine pancreas. This became apparent in autopsy material from Hordaland County, Norway, between 1972-1976, but not been seen in the preceding 15 yr. It was accompanied by an increase in multiple primary cancers. On the basis of the findings in the case-matched controls, it is concluded that the increases recorded in this autopsy material are real. (Author abstract) (6 Refs)

GONADAL TUMORS

38. PERIPHERAL VENOUS CONCENTRATIONS OF OESTROGENS IN POSTMENOPAUSAL WOMEN WITH OVARIAN CANCER.

Heinonen PK, Tuimala R, Pyykko K, Pystynen P
Dept. Obstetrics and Gynecology, Univ. Central Hosp., Tampere, Finland
Br J Obstet Gynaecol; 89(1):84-86 1982

Serum concentrations of estrone, estradiol and estriol were measured in 23 postmenopausal women, 12 with ovarian cancer and 11 with genital prolapse. Estrone (387.6 pmol/l) and estradiol (72.7 pmol/l) levels were higher in the cancer group than those in the control group (159.8 and 27.5 pmol/l respectively), while estriol levels did not differ (434.5-270.8 pmol/l). The results indicate abnormal ovarian function in postmenopausal patients with ovarian cancer. (Author abstract) (11 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

39. ADJUVANT ENDOCRINE THERAPY AND CHEMOTHERAPY FOR BREAST CANCER.

Heuson JC, Paridaens R
Clinique et Laboratoire de Cancerologie Hammaire, Institut J. Bordet, Brussels, Belgium
Rev Med Brux; 3(4):209-216 1982

Results of adjuvant therapy for breast cancer are reviewed. The concept of surgical oophorectomy was proposed as adjuvant therapy almost 100 yr ago, but two clinical trials that were published revealed that there were almost no benefits from the procedure. Castration by ovarian radiation provided benefits that were marginal at best. Early single agent chemotherapy (cyclophosphamide) provided 10% overall survival and also survival without recurrence. Best results were obtained in the 1970s with the introduction of combination adjuvant chemotherapy. Significant increases in disease-free interval were obtained, and there was a 57% reduction in failure rate and a 54% reduction in mortality. Several combination protocols worked equally well, and whether the treatment lasted 6 or 12 mo was not a critical factor. The dose that the patient received was the critical factor. Only full doses were effective in improving the survival rate in advanced breast cancer. Combination chemotherapy seemed equally effective in pre- and postmenopausal women. The effectivenes of combination chemotherapy was increased with the administration of the antiestrogen tamoxifen for estrogen-rich tumors. (23 Refs) (In FRE)

40. TREATMENT WITH A LUTEINISING-HORMONE-RELEASING-HORMONE ANALOGUE (BUSERELIN) IN PREMENOPAUSAL PATIENTS WITH METASTATIC BREAST CANCER.

Klijn JG, DeJong FH
Dr. Daniel den Hoed Kliniek, Rotterdamsch Radio-Therapeutisch Instituut, Groene Hilledijk 301, 3075 EA Rotterdam, The Netherlands
Lancet; 1(8283):1213-1216 1982

Four premenopausal women with metastatic breast cancer were treated with a potent luteinizing-hormone-releasing-hormone (LHRH) analogue as a single first-line agent. Buserelin (6-D-ser-(bu1)-LHRH-(1-9)-ethylamide) was given in very high doses intravenously and then intranasally; ovarian function did not decrease within 1-2 wk, but after this period low to very low (postmenopausal) plasma estradiol levels were reached in all patients, accompanied by flushes. Two patients, however, subsequently showed transient peaks of plasma estradiol, probably due to a persistent follicle, which lasted for some wk without a rise in plasma luteinizing hormone, follicle-stimulating hormone, or progesterone. In two patients there was no significant change in the tumor, whereas in the other two patients there was remarkable improvement. (Author abstract) (22 Refs)

41. IMMUNOREACTIVE SERUM CALCITONIN IN PATIENTS WITH MAMMARY CARCINOMA.

Fereberger W, Leb G, Passath A, Samonigg H, Beaufort F
Medizinische Klinik der Universitat, Auenbruggerplatz 11, A-8036 Graz, Austria
MMW; 124(19):471-472 1982

Serum calcitonin levels in 50 women with mammary carcinoma were measured by means of a 125I radioimmunoassay. Twenty healthy men served as controls. Bone metastases were diagnosed in 36/50 women. Elevated levels of calcitonin were found in 6/50 women; these 6 women had varying degrees of disease progression. Levels for the entire group of the patients did not differ significantly from those for the controls. Serum calcitonin is therefore not of value as a tumor marker in patients with mammary carcinoma. (9 Refs) (In GER)

42. THE MANAGEMENT OF EARLY BREAST CANCER.

Canellos GP, Hellman S, Veronesi U
Harvard Medical Sch., Boston, MA, 02115
N Engl J Med; 306(23):1430-1432 1982

Presentations, discussions, and conclusions of the November 1981 meeting of the Multidisciplinary Project on Breast Cancer of the International Union Against Cancer are summarized. Prognostic factors, local treatment, and adjuvant systemic therapy (adjuvant chemotherapy, adjuvant endocrine treatment) are discussed. Less mutilating local treatment that allows breast preservation has had some preliminary success. Adjuvant systemic therapy appears to have influenced the relapse-free survival pattern of premenopausal women; results in postmenopausal women may improve with attention to dose, dose rate, and additional hormonal therapy. (no Refs)

43. MENOPAUSAL ENDOCRINOLOGY AND MANAGEMENT.

Korenman SG
Dept. Medicine, Univ. California Los Angeles-San Fernando Valley Program, Veterans Admin. Hosp., Sepulveda, CA, 91343
Arch Intern Med; 142(6):1131-1136 1982

Entry into menopause is associated with a severe diminution of ovarian estrogen and progesterone secretion and a reduction of circulating androgens, although, in the presence of ovaries, a degree of testosterone secretion persists. Menopause is associated to a varying degree and severity, with hot flashes a disorder of central thermoregulation - progressive sex tissue atrophy, and accelerated bone mineral loss that eventually leads to a substantial prevalence of osteoporosis, with spine, hip, and radial fractures, particularly in thin, inactive smokers with low calcium intake. Treatment with estrogens eliminates hot flashes and sex tissue atrophy and prevents osteoporosis. Unfortunately, oral estrogen therapy results in overstimulation of the liver, producing secreted proteins and an increased risk of endometrial carcinoma and gallbladder disease. The addition of a progestogen will diminish the risk of endometrial carcinoma, presumably by reducing estrogen-receptor concentration and increasing estradiol dehydrogenase activity but will usually result in vaginal bleeding in women with uteri. The use of estrogen therapy with or without a progestin should be an informed joint decision of physician and patient that must be reevaluated regularly as new information becomes available. (Author abstract) (39 Refs)

44. THE EFFECT OF A POTENT LHRH ANALOGUE IN THE TREATMENT OF PROSTATIC CANCER (MEETING ABSTRACT)

Trachtenberg J, Tolis G
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Certain LHRH (luteinizing hormone-releasing hormone) analogues have been shown to markedly reduce gonadal steroidogenesis in a variety of animals. In order to assess to the effect of the chronic administration of a potent LHRH analogue, (D-

Ser(But)6)LRH(1-9)-nonapeptide-ethylamide (Hoechst, Hoe766) on prostatic tissue, adult Wistar rats were administered either 1, 3 or 13 ug of Hoe766 sc QD. At 7, 21 and 35 days of treatment, groups of animals were sacrificed and certain serum endocrine and gravimetric parameters determined. By the end of the experimental period neither serum LH nor prolactin was altered from control but serum estradiol, testicular LH receptor content, testicular weight, seminal vesicle weight, and prostate weight were markedly decreased from control; serum androgens were reduced to the castrate level. Hoe766 was also administered to 6 adult males with previously untreated metastatic prostatic cancer. Fifty ug of Hoe766 was administered sc QD or 500 ug intranasally QD for periods from 3 to 6 months. By 3 months of treatment serum prolactin and LH had not changed, but serum androgens and estradiol had declined to the castrate level and LH response to LHRH administration, serum acid phosphatase, and prostatic tumor volume as measured by pelvic ultrasound and bone scan were all markedly reduced. Hoe766 reduces serum androgens to the castrate level in both the rat and man, probably by acting at two sites, namely the pituitary (as evidenced by decreased LH response to LHRH administration) and the testis (as evidenced by decreased testicular LH receptor content). (no Refs)

45. LEUPROLIDE IN METASTATIC PROSTATIC CANCER (MEETING ABSTRACT)

Smith JA
Abbott Leuprolide Prostatic Cancer Study Group, Salt Lake City, UT
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Leuprolide is a new, potent analogue of gonadotropin releasing hormone which with chronic administration results in inhibition of pituitary release of LH and FSH (luteinizing and follicle stimulating hormones). Consequently testicular function is suppressed in men and circulating serum testosterone levels reduced. These observed endocrine effects of Leuprolide have predicated its use in prostatic cancer. One hundred and seventeen patients with metastatic prostatic cancer have been treated with Leuprolide in a multi-center Phase I-II study. Fifty-seven patients had received some form of prior endocrine treatment and 60 had no prior therapy. Patients were followed every two weeks and serial bone scans, x-rays and serum chemistries and hormones obtained according to protocol. Response criteria were those defined by the National Prostatic Cancer Project. Serum testosterone and dihydrotestosterone were suppressed to castrate levels in all patients within four weeks of the initiation of treatment. No adverse reactions or gynecomastia were encountered in any patients although most had hot flashes. Thirty previously untreated patients are evaluable to date and 70% have obtained a complete or partial objective response. An additional 27% have objectively stable disease and most patients had subjective improvement with resolution of bone pain or improvement in performance status. All responding patients are continuing on treatment. Only one patient in the previously untreated category had disease progression at week 10 of treatment. Thirty percent of patients who had relapsed on prior endocrine treatment had some subjective improvement with Leuprolide and 2 achieved an objective response. (no Refs)

46. LYMPH NODE METASTASES IN ADENOCARCINOMA OF THE PROSTATE: RESPONSE TO ENDOCRINE THERAPY (MEETING ABSTRACT)

von Eschenbach AC, Orovan WL, Zimmerman SO
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Optimal therapy has not been determined thus far for patients with adenocarcinoma of the prostate who have only lymph node metastases. The results of surgical lymphadenectomy and extended field irradiation suggest that systemic therapy is required. Fifty-seven patients ranging in age from 47 to 78 years were determined clinically to have lymph node metastases exclusively. In 34 patients only the pelvic nodes were involved (D1), while in 23 patients extrapelvic nodes were positive (D2). All patients received endocrine therapy as primary treatment of their metastatic disease. Fifty-one patients were treated with the combination of orchiectomy and diethylstilbestrol, while 6 patients received only estrogens. Follow-up ranged from 6 to 135 months. At the time of last follow-up, 31 of 57 patients were alive and free of disease, while 6 patients are alive with tumor. Only 12 patients have died as a result of cancer. The projected 5-year survival for this group is 61% with a median survival of 6.4 years. Endocrine therapy is an appropriate method of treatment for patients with nodal metastases from prostate cancer in an effort to achieve long-term cancer free survival. (no Refs)

47. EFFECTS OF TOTAL AND SUBCAPSULAR ORCHIDECTOMY ON SERUM CONCENTRATIONS OF TESTOSTERONE AND PITUITARY HORMONES IN PATIENTS WITH CARCINOMA OF THE PROSTATE.

Bergman B, Damber JE, Tomic R
Dept. Urology, Univ. Umea, S-901 85 Umea, Sweden
Urol Int; 37(2):139-144 1982

Twenty-two men with carcinoma of the prostate were consecutively subjected to either total or subcapsular orchidectomy at random. Serum concentrations of testosterone, follicle-stimulating hormone, luteinizing hormone, prolactin, thyroid-stimulating hormone and testosterone-estrogen-binding globulin were followed. No differences were found between the two groups during the 6-mo follow up period. Orchidectomy reduced testosterone concentration in all cases and none responded to human chorionic gonadotrophin stimulation 6 mo postoperatively. The concentrations of free and bound testosterone were calculated but did not vary between the two types of operation, which were considered equally efficient in reducing testosterone concentration. However, doubts about the completeness of the operation might possibly arise in cases with cancer progress and therefore we prefer total orchidectomy as the first choice, but perform subtotal orchidectomy on those men preferring this type of operation psychologically. (Author abstract) (20 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

48. EFFECT OF HYPOTHALAMIC AND PITUITARY IRRADIATION ON PUBERTAL DEVELOPMENT IN CHILDREN WITH CRANIAL TUMORS.

Rappaport R, Brauner R, Czernichow P, Thibaud E, Renier D, Zucker JM, Lemerle J
Hopital des Enfants Malades, 149, rue de Sevres, 75730 Paris Cedex 15, France
J Clin Endocrinol Metab; 54(6):1164-1168 1982

The purpose of the present study was to report on gonadotropin function and puberty of a large group of children treated by cranial irradiation for cranial and neck tumors and medulloblastoma. Forty-five children of pubertal age were investigated. The mean interval time since radiation was 5 2/12 yr. Gonadotropin and gonadal function were evaluated by clinical criteria, plasma sex steroids, and plasma LH and FSH responses to LRH. Puberty was complete or progressing normally in 31 cases and was abnormal in 14 cases. Severe gonadotropin deficiency, with lack of or slow progression of puberty and decreased LH and FSH responsiveness to LRH, was observed in five cases; two of these had moderately elevated plasma PRL levels. Secondary amenorrhea or lack of pubertal progression was found in five other cases. GH deficiency was associated with gonadotropin deficiency in 9 of these 10 cases. Adrenal function, estimated by basal dehydroisoepiandrosterone, dehydroisoepiandrosterone sulfate, and estrone, was normal according to pubic hair stages. In conclusion, complete or partial gonadotropin deficiency can be the consequence of cranial irradiation in children receiving 6,000 rads or less. It is usually associated with GH deficiency. The site of the damage on the pituitary gland or the hypothalamus remains to be demonstrated. (Author abstract) (22 Refs)

49. LATE EFFECTS OF RADIATION THERAPY IN THE TREATMENT OF HODGKIN'S DISEASE.

Kinsella TJ, Fraass BA, Glatstein E
Radiation Oncology Branch, Div. Cancer Treatment, NCI, NIH, Building 10, Rm B3B38, Bethesda, MD, 20205
Cancer Treat Rep; 66(4):991-1001 1982

In the last two decades, a considerable amount of clinical and experimental animal data has been accumulated regarding the tolerance of the major normal tissues and organs traversed by the radiation beams in treating Hodgkin's disease. Typically, the tolerance of several tissues and organs must be considered in designing the very large radiation portals such as the mantle. Today, sophisticated machinery such as computerized tomography scanners, simulators, computers, and linear accelerators are available to improve the radiation planning and treatment of Hodgkin's disease. In this paper, we discuss the late effects of radiation therapy to the lung, heart, thyroid, kidney, gastrointestinal tract, and the gonads of adults with Hodgkin's disease. Emphasis is placed on our recommendations for modifications of radiation technique to improve the complication-free cure rate. (Author abstract) (47 Refs)

50. SCLEROSING HEPATIC CARCINOMA: RELATIONSHIP TO HYPERCALCEMIA.

Omata M, Peters RL, Tatter D
(c/o Peters) USC Liver Unit - Pathology, Rancho Los Amigos Hosp., 7705 Golondrinas, 1200 Building, Downey, CA, 90242
Liver; 1(1):33-49 1981

A series of 30 patients with primary liver tumors of a distinctive histological pattern designated primary sclerosing hepatic carcinoma (SHC) were observed in a 25 yr period. Comparison of clinical data and autopsy findings were made with those of 46 patients dying of hepatocellular carcinoma (HCC) and 9 dying of primary peripheral cholangiocarcinoma (PCC). No significant differences in liver and spleen wt were found between the three tumor types. SHC was characterized grossly by abundance of uniformly dense fibrous tissue. The most characteristic feature of SHC was the tendency to be associated with fibrous tissue which surrounded slender cords of neoplastic cells. At the margins of the neoplasm, tumor cells often blended with nonneoplastic cells; nonneoplastic hepatocytes often coexisted in the same hepatic cord. Eleven of 16 SHC patients tested had elevated serum calcium levels (SCAL). Only one of these 11 patients with hypercalcemia had a bone metastasis. In a total of 38 patients with either HCC or PCC, only 2 (5.3%) had hypercalcemia, and both had bone metastases. Thus, no patient with classical HCC or PCC had bone metastases without hypercalcemia. The mean SCAL in patients with SHC was significantly higher than in those with HCC and PCC. Characteristics of clinical features and comparison of laboratory findings in SHC, HCC, and PCC patients are presented. Analysis of clinical data in conjunction with comparison of two other major primary hepatic tumors indicated that SHC is a neoplasm with features intermediate between HCC and PCC, including some morphologic features of either or both. (41 Refs)

51. CHANGES IN THE DIAGNOSIS AND TREATMENT OF ZOLLINGER-ELLISON SYNDROME.

Feurle GE, Helmstadter V, Hoevels J, Wenzel-Herzer G, Klempa I
Medizinische Universitats-Poliklinik, Hospitalstr. 3, 6900 Heidelberg 1, W. Germany
Dtsch Med Wochenschr; 107(18):697-704 1982

A gastrinoma was found in 12 of 23 patients with Zollinger-Ellison syndrome. Those with gastrinoma were not different from those without as regarded fasting gastrin level, increased gastrin secretion after secretin and calcium, acid secretion, or survival time. Five of the 23 patients have died, 4 immediately postoperatively, the 5th of the metastasizing tumor. Treatment with the H2-receptor antagonist cimetidine avoided emergency operation and thus decreased operative mortality, giving time for localization by ultrasound, computed tomography and selective arteriography. The rate of false-negative results was high. Transhepatic selective catheterization of the pancreatic veins with gastrin determination gives localization of the tumor and identification of the secreted hormone. In three patients tumor resection was possible under cover of H2-receptor antagonist administration which normalized gastrin and acid secretion. There is a change in the treatment of the Zollinger-Ellison syndrome, away from total gastrectomy to conservative treatment with H2-receptor antagonists and an attempt of curative treatment by removal of the tumor. (Author abstract) (39 Refs) (In GER)

52. THE DIFFUSE ENDOCRINE SYSTEM AND CARCINOIDS OF THE GASTROINTESTINAL TRACT: PART 1: ORTHOLOGICAL VIEWPOINTS AND GENERAL PATHOLOGY OF CARCINOIDS.

Borchard F
Pathologische Institut, Universitat Dusseldorf, Moorenstr. 5, D-4000 Dusseldorf, W. Germany
Z Gastroenterol; 20(4):187-205 1982

Carcinoids are epithelial tumors of the gastrointestinal tract that have potential endocrine activity and may become malignant. Eighteen distinct cell types have been identified, varying in histological structure, reactivity to silver salts, and the number and type of endocrine products. Small-cell anaplastic carcinomas contain endocrine granules and are highly malignant. Normal cells and carcinoids may exhibit a mixture of endocrine and exocrine differentiation. (87 Refs) (In GER)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

53. MALIGNANCY - METABOLIC MANIFESTATIONS OF CANCER.

Coombes RC
Ludwig Inst. for Cancer Res., London, England
J Appl Med; 8(5):361,363-365,367-368 1982

Cancer associated hormone-mediated syndromes are reviewed with reference to their possible role as tumor markers. Cushing's syndrome may be associated with small cell lung cancer and the syndrome of inappropriate antidiuretic hormone secretion is often associated with small cell carcinoma of the bronchus or a carcinoid tumor. Hypocalcemia, gynecomastic, hypertrophic osteoarthropathy, acromegaly, cachexia, hypoglycemia, gastrointestinal syndrome and neurological complications are all cancer-associated pathologies. (33 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

54. PITUITARY RESPONSES TO THYROTROPIN-RELEASING HORMONE AFTER TREATMENT WITH THE BREAST CARCINOGEN NITROSOMETHYLUREA: INHIBITION OF PROLACTIN BUT NOT THYROTROPIN RELEASE.

Kieffer JD, Maloof F, Vickery AL, Mover H, Downing M, Ridgway EC
Thyroid Unit, Massachusetts General Hosp., Boston, MA, 02114
Endocrinology; 110(6):1892-1896 1982

N-Nitrosomethylurea (NMU) is a widely used experimental breast carcinogen. The present report describes the effects of NMU on the plasma PRL and TSH increases in response to exogenous TRH. Female Buffalo rats, 75-80 days old, were given a single ip injection of NMU (10 mg/100 g) or vehicle. At various times after injection, NMU-treated rats and vehicle-injected controls were tested with exogenous TRH (625 ng/100 g, ip). Groups of four to six rats were bled at 10, 20, 30, 45, and 60 min after TRH and at 10 min after saline (baseline group). The response to TRH (delta) was determined by subtracting the mean plasma PRL or TSH level of the baseline group from the mean peak level observed after TRH. For four separate control experiments, deltaPRL averaged 104 +-19 ng/ml (mean +- SE). At 20 hr, 42 hr, 6 days, and 2, 3, 4, 8, and 12 wk after NMU, deltaPRL was 87, 0, 0, 16, 10, 3, 49, and 65 ng/ml, respectively. deltaPRL was statistically significant in all four control experiments, and remained significant at 20 hr after NMU. However, from 42 hr through 4 wk, no significant deltaPRL occurred. A significant deltaPRL reappeared at 8 and 12 wk, the approximate time of appearance of the first palpable breast cancers. Pituitary PRL concentrations (micrograms PRL per mg protein) were significantly lower in NMU-treated groups than in vehicle-treated controls at 42 hr, 3 wk, and 12 wk. In contrast to its marked inhibitory effect on deltaPRL, NMU had no effect on deltaTSH. This is consistent with the hypothesis that treatment with NMU resulted in a selective impairment of pituitary PRL-secreting cells. Moreover, our data show that the plasma PRL response to TRH was inhibited at times after NMU when pituitary PRL was not significantly depleted. This observation is in accord with the concept of impairment of either TRH receptor binding or events which couple receptor binding and hormone release. (Author abstract) (38 Refs)

55. THYROTROPIN BINDING AND ADENYLATE CYCLASE ACTIVATION IN NORMAL AND NEOPLASTIC HUMAN THYROID TISSUE: LACK OF EFFECT OF THYROGLOBULIN.

Clark OH, Gerend PL, Nissenson RA
Surgical Service (112), Veterans Admin. Medical Center, 4150 Clement St., San Francisco, CA, 94121
J Clin Endocrinol Metab; 54(6):1157-1163 1982

The effects of bovine TSH (bTSH) and bovine (bTg) and human thyroglobulin (hTg) on the binding of [125I]bTSH and the activation of adenylate cyclase (AC) were studied in both normal and neoplastic human thyroid homogenates in vitro using adenylate cyclase conditions. [125I]bTSH bound specifically and with high affinity to a particulate fraction from normal thyroid and from benign and malignant thyroid neoplasms; this binding was inhibited by unlabeled bTSH (approx Kd = 10.0 mU/ml for normal tissue; Kd = 2.5 mU/ml for thyroid neoplasms). Half-maximal activation of AC was obtained at a TSH concentration of approx 2.5 mU/ml for both normal and neoplastic thyroid tissue, indicating that the high affinity TSH receptors are coupled to AC, at least in the neoplastic thyroid tissue. bTg and hTg did not inhibit [125I]bTSH binding to high affinity TSH receptors in either normal or neoplastic thyroid tissue. bTSH increased AC activity up to 25-fold in neoplastic thyroid tissue and up to 4-fold in normal thyroid tissue, whereas at concentrations up to 1 mg/ml, bTg had no effect. The current study demonstrates that bTSH binds to specific, high affinity receptors and stimulates AC activity in both normal and neoplastic thyroid tissue. bTg and hTg, under the conditions used in this experiment, do not influence TSH binding to its high affinity receptor in these tissues. Since Tg does not influence high affinity TSH binding or AC activity in a particulate fraction rich in plasma membranes from normal or neoplastic thyroid tissue, it is unlikely to have a modulating role on TSH action at the thyroid plasma membrane. (Author abstract) (26 Refs)

56. LONG-TERM EFFECT OF RADIATION ON THYROID FUNCTION AND TUMOR FORMATION.

Prinz RA, Oslapas R, Hofmann C, Shah KH, Ernst K, Refsguard J, Lawrence AM, Paloyan E
Res. Service, Hines Veterans Admin. Hosp., Hines, IL, 60141
J Surg Res; 32(4):329-337 1982

Cellular injury coupled with hypersecretion of thyroid stimulating hormone (TSH) is considered the mechanism for radiation-induced thyroid tumors. This hypothesis was tested by administering 40 uCi of 131I to male and female rats. Serum thyroxine (T4) decreased significantly overtime in male and female control and radiated animals. T4 was essentially the same in 6-and 12-mo-old radiated and control animals, but a significant decrease in T4 was noted in radiated females at 21 mo. TSH decreased overtime in control animals, but a significant increase in TSH was required in radiated animals to maintain T4 levels. Thyrocalcitonin (TC) was significantly greater in 21-mo-old control females than in males or radiated females. A significant increase in follicular cell thyroid neoplasms in radiated animals was associated with the elevated TSH levels. The importance of sex in thyroid tumor formation is illustrated by the fact that males had a significantly higher frequency of thyroid neoplasms than did females. C-cell hyperplasia and medullary thyroid carcinoma only occurred in control animals and accounted for their higher TC levels. This study confirms that administration of low doses of 131I leads to an increased frequency of thyroid tumor formation in rats and that direct cellular injury plus hypersecretion of TSH seem responsible for these radiation-induced tumors. (Author abstract) (18 Refs)

57. INSULIN RELEASE AND PROTEIN PHOSPHORYLATION: POSSIBLE ROLE OF CALMODULIN.

Schubart UK, Erlichman J, Fleischer N
Dept. Medicine and Diabetes Res. and Training Center, Albert Einstein Coll. Medicine, Bronx, NY, 10461
Fed Proc; 41(7):2278-2282 1982

Both Ca++ and cyclic AMP (cAMP) are implicated in the regulation of insulin release in the pancreatic beta cell. In hamster insulinoma cells used in our laboratory to study the mechanism of insulin release, Ca++ and cAMP trigger secretion independently. Concomitant with stimulation of the secretory apparatus both cAMP and Ca++ promote phosphorylation of distinct insulinoma cell proteins. Calmodulin may be involved in the stimulation of insulin release and protein phosphorylation induced by Ca++ influx. The Ca++-dependent protein kinase of the insulinoma cell is activated by exogenous calmodulin and blocked by trifluoperazine, an inhibitor of calmodulin action. This drug also inhibits glucose-induced insulin release in pancreatic islets. In insulinoma cells trifluoperazine blocks Ca++ influx-mediated insulin release and protein phosphorylation with no effect on basal or cAMP-mediated secretion. Inhibition of Ca++ influx-mediated insulin release and protein phosphorylation occurs with nearly identical dose dependence. Inasmuch as trifluoperazine affects voltage-dependent Ca++ uptake in insulinoma cells, an involvement of calmodulin cannot be directly inferred. The evidence suggests that protein phosphorylation may be involved in the activation of the secretory apparatus by both cAMP and Ca++. It is proposed that stimulation of insulin release by cAMP and Ca++ is mediated by cAMP-dependent protein kinase and calmodulin-dependent protein kinase, respectively. (Author abstract) (43 Refs)

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Diagnosis, Treatment, Pathophysiology

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NOVEMBER, 1982

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Consulting reviewer:
NAGUIB A. SAMAAN, M.D., Ph.D.

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. REGIONS OF LOW DENSITY IN THE CONTRAST-ENHANCED PITUITARY GLAND: NORMAL AND PATHOLOGIC PROCESSES.

Chambers EF, Turski PA, LaMasters D, Newton TH
Dept. Radiology, Univ. California Sch. Medicine, San Francisco, CA, 94143
Radiology; 144(1):109-113 1982

The incidence of low-density regions in the contrast-enhanced pituitary gland and the possible causes of these regions were investigated by a retrospective review of computed tomographic (CT) scans of the head in 50 patients and autopsy specimens of the pituitary in 100 other patients. It was found that focal areas of low density within the contrast-enhanced pituitary gland can be caused by various normal and pathologic conditions such as pituitary microadenomas, pars intermedia cysts, foci of metastasis, infarcts, epidermoid cysts, and abscesses. Although most focal low-density regions probably represent pituitary microadenomas, careful clinical correlation is needed to establish a diagnosis. (Author abstract) (19 Refs)

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2. THE ACROMEGALY SYNDROME. RELATION BETWEEN CLINICAL FEATURES, GROWTH HORMONE VALUES AND RADIOLOGICAL CHARACTERISTICS OF THE PITUITARY TUMOURS.

Jadresic A, Banks LM, Child DF, Diamant L, Doyle FH, Fraser TR, Joplin GF
Endocrine Unit, Hammersmith Hosp., London W12 0HS, England
Q J Med; 51(202):189-204 1982

One hundred and fifty-five acromegalies, 76 males (mean age 44 +-1.3 yr) and 79 females (45 +-1.4 yr) were studied. The frequency of clinical features were: acral enlargement 100%, hyperhidrosis 65%, headache 55%, paraesthesiae 49%, cardiac problems 34%, hypertension 32%, diabetes mellitus (clinical and chemical) 27%, and visual field defects 6%. Signs and symptoms, and particularly headache, did not show any relation with the size or shape of pituitary tumors, nor with growth hormone (GH) values, age, sex or weight. Mean of GH values at 60, 90 and 120 min during a GTT averaged 135 mIU/l, range 8-1,833. Diabetes mellitus was more frequent and severe in patients with higher GH values, occurring in 32% of patients with mean GH values greater than or equal to 50 mIU/l and only in 16% of the rest (p less than 0.05). GH values correlated positively with size of tumors. Forty-nine percent of patients presented with entirely intrasellar tumors, 27% with suprasellar extensions and 23% with partially empty sellae. The mean GH (238 mIU/l) of patients with suprasellar extensions was significantly higher (p less than 0.004) than those of the others. Younger acromegalies showed a tendency to larger tumors. Early treatment of acromegaly, particularly in young patients and those presenting with high GH values, is recommended. (Author abstract) (61 Refs)

3. LIMITED VALUE OF OPHTHALMOLOGICAL EXAMINATIONS FOR DETECTION OF RECURRENT PITUITARY ADENOMA.

Mehdorn E, Kommerell G
Abteilung fur Neuro-Ophthalmologie und Schielbehandlung, Univ.-Augenklinik, Killianstrasse 5, 7800 Freiburg, W. Germany
Klin Monatsbl Augenheilkd; 180(4):275-278 1982

Three patients (a man 47-yr-old and 2 women 57-and 42-yr-old) were subjected to ophthalmological follow-up examinations after surgery for pituitary gland adenomas. The ophthalmological examinations were unable to detect the recurrences, because they occurred in areas where the optic nerve had already been destroyed by the primary tumor. Suprasellar recurrences were diagnosed by computer tomography in all three patients. The findings indicate that unchanged visual fields do not rule out tumor recurrence and that computer tomography is indispensable in the follow-up of surgically treated patients with pituitary adenomas. (29 Refs) (In GER)

4. OPERATIVE MANAGEMENT OF CHROMOPHOBE PITUITARY TUMOUR RECURRENCES.

Valtonen S, Salmi J
Dept. Neurosurgery, Helsinki Univ. Central Hosp., Topeliuksenkatu 5, SF-00260 Helsinki 26, Finland
Acta Neurochir (Wien); 62(3/4):233-240 1982

Twenty-three operations were performed for recurrences of previously treated chromophobe pituitary adenomas. Eleven operations were transcranial, ad 12 were transsphenoidal. Twenty-two patients were operated on because of deteriorating eyesight; this improved in 10 patients, deteriorated further in 3, and did not significantly change in the remaining 9 patients. There was one postoperative death. The patients generally had hypopituitarism already at the time of diagnosis, and it tended to increase during treatment. The results are certainly worse than after primary operations, but there is no alternative for handling a sizeable recurrence that has already affected the optic pathways. (Author abstract) (15 Refs)

5. TRANSSPHENOIDAL MICROSURGERY OF SELLAR-PARASELLAR CHORDOMAS.

Takahashi T, Kuwayama A, Kobayashi T, Watanabe M, Katoh T, Kageyama N
Dept. Neurosurgery, Nagoya Univ., 65 Tsurumai-cho, Showa-ku, Nagoya 460, Japan
Neurol Med Chir (Tokyo); 22(2):141-146 1982

Two cases of sellar-parasellar chordomas were experienced, the main symptoms of which were slowly progressive cranial nerve palsies. Localized destruction of the sella turcica and a soft tissue mass protruding into the sphenoid sinus detected by CT and hypocycloid tomography were suggestive of sellar-parasellar chordomas. Endocrinological findings, size of the sella turcica and findings on contrast enhanced CT were helpful in differentiating them from pituitary adenomas. Cerebral angiography, metrizamide CT and hypocycloid tomography of the sella turcica suggested that the main mass was restricted to the epidural spaces, infiltrating into the sphenoid bone. The authors adopted transsphenoidal microsurgery, rather than craniotomy, to avoid injury to the dura mater and dissemination of the tumor cells in the cerebrospinal fluid pathway. The tumors were soft with few vessels and they were easily removed by suction and curettage, preserving the dura mater intact. (Author abstract) (30 Refs) (In JPN)

6. TOLERANCE OF THE CENTRAL NERVOUS SYSTEM TO PHOTON IRRADIATION. ENDOCRINE COMPLICATIONS.

Wigg DR, Murray RM, Koschel K
Radiotherapy Dept., Royal Adelaide Hosp., North Terrace, Adelaide 5000, Australia
Acta Radiol Oncol Radiat Phys Biol; 21(1):49-60 1982

Dose-response isoeffect equations have been determined for hypothalamic pituitary insufficiency following cranial irradiation. Of particular importance is the occurrence of complications at doses substantially less than those commonly used for the treatment of central nervous system tumors. Such complications may be severe and potentially life threatening. These complications occur when a small midline 'target' vol containing the pituitary gland, infundibulum and adjacent inferior hypothalamic structures is irradiated. Direct pituitary irradiation is unlikely to be a factor, at least in some cases. The possible role of incidental hypothalamic irradiation in the control of acromegaly and pituitary dependent Cushing's syndrome is discussed. (Author abstract) (53 Refs)

7. THE PLACE OF BROMOCRIPTINE IN THE TREATMENT OF ENDOCRINE DISORDERS.

Althoff PH, Bottger B, Rosak C, Jungmann E, Neubauer M
Abteilung fur Endokrinologie, Zentrum der Inneren Medizin, Universitat Frankfurt am Main, Theodor-Stern-Kai, D-6000 Frankfurt/Main 70, W. Germany
Inn Med; 9(4):189-198 1982

Bromocriptine (BC) is a long-acting dopamine-agonist used in treatment of endocrinologic diseases of functional or organic origin. In patients with hyperprolactinemia chronic stimulation of dopamine-receptors by BC rapidly lowers serum prolactin level. Indications for BC therapy include acromegaly, prolactinoma, and idiopathic edema. Although BC apparently has no acute toxicity, numerous side effect may be produced by BC therapy. (13 Refs) (In GER)

8. BROMOCRIPTINE IN MANAGEMENT OF LARGE PITUITARY TUMOURS.

Wass JA, Williams J, Charlesworth M, Kingsley DP, Halliday AM, Doniach I, Rees LH, McDonald WI, Besser GM
Dept. Endocrinology, St. Bartholomew's Hosp., London EC1A 7BE, England
Br Med J; 284(6333):1908-1911 1982

Bromocriptine has an accepted place in the management of small pituitary tumors that secrete either prolactin or growth hormone. The treatment of large tumors with extrasellar extensions is more difficult, however: though surgery is the standard treatment, it is often unsuccessful in returning excessive hormone secretion to normal and may cause hypopituitarism. A prospective trial was undertaken to assess the frequency with which changes in pituitary function and size of large tumors occurs. Nineteen patients were studied before and during treatment with bromocriptine (7.5 to 60 mg/day) for 3 to 22 mo, using contrast radiology and a detailed assessment of pituitary function. Eighteen patients had hyperprolactinemia and 2 of these also had raised concentrations of growth hormone; 1 patient had an apparently non-functioning tumor. In 12 patients (63%) tumor size decreased with bromocriptine and no tumor enlarged. Nine patients had visual-field defects, which improved in seven, becoming normal in five. Pituitary function improved in nine patients (47%) becoming entirely normal in three. Bromocriptine should be the treatment of choice in patients with large pituitary tumors with extrasellar extensions, provided close supervision is maintained. (Author abstract) (35 Refs)

9. MEDICINAL THERAPY OF PITUITARY TUMORS.

Hesch RD, Wagner TO
Abteilung fur Klinische Endokrinologie, Zentrum fur Innere Medizin, Medizinische Hochschule, Karl-Wiechert-Allee 9, D-3000 Hannover, W. Germany
Dtsch Med Wochenschr; 107(23):883-886 1982

The current status of medicinal therapy of pituitary tumors is discussed. Preadenomatous hyperprolactinemia and prolactinoma may be treated with bromocriptine (BC). BC can produce a reduction in size of the tumor as well as a reduction in serum levels of prolactin. If the tumor does not respond to BC, surgery may be required. BC can be used for prevention of recurrences of prolactinoma. For the treatment of growth hormone- or ACTH-producing tumors or of hormonally inactive tumors, BC has not been shown to be sufficiently effective to replace surgery. (17 Refs) (In GER)

10. LYMPHOID ADENOHYPOPHYSITIS WITH RADIOLOGIC AND CLINICAL FINDINGS RESEMBLING A PITUITARY TUMOR.

Hungerford GD, Biggs PJ, Levine JH, Shelley BE, Perot PL, Chambers JK
Dept. Radiology, Medical Univ. South Carolina, 171 Ashley Ave., Charleston, SC, 29425
AJNR; 3(4):444-446 1982

Difficulties encountered in differential diagnosis of lymphoid adenohypophysitis in a 27-yr-old woman are reported. The patient was seen with severe parietal headache and blurred vision. Computed tomography showed a mass in the sella and suprasellar region. The patient was subjected to bifrontal craniotomy and removal of the firm mass with unusual grayish-yellow appearance. Histological examination of the surgery specimen indicated lymphoid infiltration of the adenohypophysis. (19 Refs)

THYROID TUMORS

11. FINE NEEDLE ASPIRATION OF THE THYROID - REVIEW OF A VALUABLE DIAGNOSTIC TECHNIQUE.

Walts AE
Div. Anatomic Pathology, Cytopathology Section, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, CA, 90048
Clin Otolaryngol; 7(3):205-214 1982

Advantages, limitations, and diagnostic criteria of fine needle aspiration of the thyroid are reviewed. The technique is described. The most important technical factors are proper localization of the needle, multiple multidirectional aspirations, and rapid fixation. A malignant diagnosis should never be made on other than several well preserved cells; at least 8-10 well preserved epithelial cell groups per two slides is adequate. Pertinent clinical data include single vs multiple nodules, 'cold' vs 'hot' nodules, solid vs cystic vs mixed nodules, size and change in size of nodules, functional state of the gland, a history of irradiation to the head and neck, a family history of thyroid carcinoma, and the site of aspiration. Principle cytologic features of benign thyroid lesions are described, including follicular adenoma, hyperplasia, Hashimoto's thyroiditis, cysts, and others. Cytologic features of malignant thyroid lesions are listed and described, including papillary carcinoma, follicular carcinoma, lymphoma, squamous carcinoma, medullary carcinoma, and giant cell (anaplastic) carcinoma. (23 Refs)

12. SOLITARY THYROID NODULES IN CHILDREN AND ADOLESCENTS.

Hung W, August GP, Randolph JG, Schisgall RM, Chandra R
Children's Hosp. Natl. Medical Center, 111 Michigan Ave., N.W., Washington, DC, 20010
J Pediatr Surg; 17(3):225-229 1982

Thirty-nine children and adolescents with a solitary nodule of the thyroid gland were seen over a 16-yr period and 35 had their nodules removed surgically. All of the patients had preoperative thyroid scintiscans, of which 27 showed a cold nodule. The most common cause of solitary thyroid nodules was follicular adenoma. Five of the 27 cold nodules were malignant (18.5%) while no malignancies were present in the warm or hot nodules. Available diagnostic methods of attempting differentiation of benign from malignant solitary nodules are reviewed and an approach to the clinical management of such nodules as derived from our experience is presented. (Author abstract) (21 Refs)

13. PAPILLARY CARCINOMA OF THE THYROID GLAND: A CLINICO-PATHOLOGICAL STUDY OF 123 CASES.

Shrikhande SS, Phadke AA
Dept. Pathology, Tata Memorial Hosp., Parel, Bombay 400 012, India
Indian J Cancer; 19(2):87-92 1982

A clinical and pathological study is presented of 123 cases of papillary carcinoma of the thyroid with some stress upon those cases which represent pure carcinoma and those that are mixed papillary and follicular carcinoma. Ages of the patients ranged from 6 yr to 76 yr; 42 were males, 81 females. In terms of diagnosis, the thyroid scan, frozen section, and lymph node biopsy were all found useful. Hemithyroidectomy was carried out in 45 cases, total thyroidectomy in 45 cases. In the remaining 29 cases total thyroidectomy was combined with radical neck dissection. Adequate postoperative follow-up was available in 109 cases. No significant difference was found in the incidence of regional lymph node metastasis or distant metastasis within the pure papillary and mixed papillary and follicular tumor groups. Only nine deaths have occurred, only one of which was related to the carcinoma (pressure upon the trachea). In the remaining eight cases, the cause of death was unrelated to thyroid carcinoma in four cases and was not known in the other four cases. (15 Refs)

14. A CLINICAL AND STATISTICAL STUDY OF 274 OPERATIONS FOR THYROID CANCER.

Marchegiani C, Custureri F, Lucci S, Carbonara G, Angelini R, Marandola S, Nobili M, Carratu C, Romani AM, Macri S
V Clinica Chirurgica, Universita Studi Roma, Roma, Italy
Minerva Chir; 37(8):737-744 1982

A series of 274 thyroid neoplasia operations performed from 1970 to 1980 are discussed. The cases are part of a total series of 2,519 operations for thyropathy, with a 10.87% incidence of neoplasia. 199 of the 274 patients were women, the remaining 75 were men. The incidence of cancer for the males (11.62%) was slightly higher than for the females (10.61%). All but 18 patients underwent total surgery. In the first age group (0-10 years) all thyroid pathologies that underwent surgery were found to be cancerous (100%). This percentage decreased to 21.80% in the second age group (11-20 years) and to 10.60% in the third group (21-30 years), reaching its lowest level, 6.07% during the fourth decade of life. A gradual increase in the incidence of thyroid cancer was observed from the fifth to the eight decade of life. These values were reported at 8.65%, 10.40%, 19.10% and 33.33%, respectively. The histological variety of the tumors were equally distributed between the age groups. However, a relative increase in the incidence of undifferentiated tumors was detected in older patients. The incidence of undifferentiated tumors, almost absent in the first two decades of life, became 15.4% in the fourth decade, and rose to 25% in the sixth, 40% in the seventh and 60% in the eight. It was concluded that cancer of the thyroid must be considered a disease with a precise diagnostic and a treatment protocol which is not based upon improvisation but depends upon histological and endocrinologic analysis, biologic testing and nuclear medicine in addition to surgical procedures. (36 Refs) (In ITA)

15. OPERATIVE STRATEGY IN NONFAMILIAL MEDULLARY THYROID CARCINOMA.

Braun J, Raguse T
Abteilung Chirurgie der Medizinischen Fakultat, RWTH Aachen, Goethestr. 27/29, D-5100 Aachen, W. Germany
Aktuel Chir; 17(3):77-81 1982

Nonfamilial medullary thyroid carcinoma (MTC) in 12 patients (2 men, 10 women; 30-75 yr old) is reported. Six of the patients had firm, nodular goiters; six had unilateral, mobile, solitary tumors. Scintigraphy showed cold nodes in 10 of the patients; no distant metastases were detected in any. Diagnosis of MTC was based on intraoperative rapid-section examination in 10 patients and paraffin-section examination in 2. Radical neck dissection (RND) was performed whenever surgically removed lymph nodes were not free of tumor. Surgical therapy consisted of lobectomy in two patients, nearly complete thyroidectomy in five (including 2 with RND), total thyroidectomy in three (including 2 with RND), and palliative measures in two. Examination of surgical specimens from each patient showed trabecular cell formations, with various anaplastic cell forms. No bilateral, multicentric tumors were found. Of 10 curatively treated patients, 5 developed recurrent tumor 3-19 mo after the first surgical procedure. Recurrences developed only in patients in whom RND was not sufficiently radical. Eight of the 12 patients died during an observation period of greater than 5 yr; 1 of these died of cardiac infarction. Four patients were alive and free of recurrence 5 yr after the surgery. (39 Refs) (In GER)

16. SURVIVAL TIME AND 'CURE' IN PAPILLARY AND FOLLICULAR THYROID CARCINOMA WITH DISTANT METASTASES: STATISTICS FOLLOWING UNIVERSITY OF MICHIGAN THERAPY.

Beierwaltes WH, Nishiyama RH, Thompson NW, Copp JE, Kubo A
Nuclear Medicine Div., Univ. Michigan Medical Center, Box 021, 1405 E. Ann St., W5629, Ann Arbor, MI, 48109
J Nucl Med; 23(7):561-568 1982

Between 1947 and 1980, 103 patients with well-differentiated thyroid carcinoma with metastases outside the neck were treated with sodium iodide (I-131) after surgical treatment. Forty-one patients had distant metastases first detected an av of 7.44 yr after the initial operation establishing the diagnosis of thyroid carcinoma. Follicular and papillary carcinomas gave the same survival time in patients, matched for age and sex, who had metastases outside the neck. Those considered to be free of their metastatic disease after I-131 therapy survived 3x as long as those with persistent disease. Patients freed of their metastases had a higher conformity rate with half of our 10 procedures of 'ideal' treatment, compared with patients not freed of their metastases. (Author abstract) (14 Refs)

17. TWO-ORTHOGONAL-VIEW METHOD FOR QUANTIFICATION OF RAD DOSE TO NECK LESIONS IN THYROID CANCER THERAPY PATIENTS.

Koral KF, Adler RS, Carey JE, Kline RC, Beierwaltes WH
Dept. Internal Medicine, Div. Nuclear Medicine, Univ. Michigan Medical Center, Ann Arbor, MI, 48109
Med Phys; 9(4):497-505 1982

A new technique is described for the determination of the dose in rad to metastatic lesions in the neck following administration of 131I for the treatment of thyroid carcinoma. The technique utilizes a high-energy pinhole collimator mounted on an Anger camera which can be rotated to record lateral and anterior views from known positions relative to the patient. A new algorithm is derived for the determination of lesion location in three dimensions, utilizing the distance of closest approach between back-projected rays from the two views. In addition, a new derivation is presented for the estimation of ellipsoid volume from two pinhole projections. The method makes use of a computer edge detection program to delineate the projected lesion boundaries. The output is either a mean estimate from one view or a more definitive upper bound derived from both views. The uptake in counts is determined from daily anterior images which are corrected for pinhole efficiency falloff with distance. This uptake is converted into microcuries by use of an in-air calibration curve. An attenuation correction is applied using the calculated lesion depth and an assumed attenuation coefficient. The dose rate is calculated using standard assumptions and is integrated graphically over the first few days when the rate peaks and by utilizing a singledecaying-exponential fit to the data over the remaining days. Illustrative patient data are presented in which doses are calculated for three neck lesions after an administration of 175 mCi of 131I. These doses include a lower bound of 2,400 rad and estimates of 5,300 and 9,500 rad. (Author abstract) (9 Refs)

18. COEXISTENCE OF HYPERTHYROIDISM AND THYROID CANCER.

Wahl RA, Goretzki P, Meybier H, Nitschke J, Linder M, Rober HD, Thomas CG
Zentrum fur Operative Medizin I, Chirurgische Klinik, Robert-Koch-Strasse 8, 3550 Marburg, W. Germany
World J Surg; 6(4):385-390 1982

Coexistence of hyperthyroidism (HT) and thyroid cancer (TC) was analyzed retrospectively using data from three surgical centers in endemic regions of West Germany. TC was demonstrated histologically in 18/702 (2.6%) patients who underwent surgery for HT. Five additional patients were found to be hyperthyroid preoperatively, making a total of 23 cases with coexistent HC and TC. These 23 patients with coexistent TC and HT represent 4.2% of 554 patients treated for TC. Higher incidence of TC was observed in patients with multinodular toxic goiters (TG; 3.3% of 317 patients) and uninodular TG (2.9% of 207). The highest incidence of HT in TC was observed in papillary (13/152 patients) and follicular TC (9/200). The sex ratio indicated a strong female preference (10.5:1). The age distribution did not differ from that of TC without HT. Fifteen of 23 patients had intrathyroidal primary lesions without macroscopic metastases. In three patients, large inoperable infiltrating and metastatic tumor masses existed. TC was located within a solitary toxic nodule in six patients, outside a solitary toxic nodule in four, and within a multinodular toxic goiter containing a variety of hot and cold areas in eight. In two patients with Graves' disease, microscopic dissemination was observed. Malignancy in those with coexistent HC and TC was diagnosed preoperatively in only 5/23 patients and only in those with advanced tumor stages. Data indicated that coexistence of HT and TC is more frequent than was observed in former studies. (25 Refs)

19. RADIATION AND RISK FOR THYROID CANCER: ATYPICAL FINDINGS OF A COMMUNITY THYROID RECALL PROGRAM.

Straub W, Miller M, Sanislow C, Fishbeck W
Dept. Radiology, Midland Hosp. Center, Midland, MI, 48640
Clin Nucl Med; 7(6):272-276 1982

Screening of 553 persons for thyroid disease by scan and physical exam was performed. Group I (245) had documented irradiation, with most (85%) receiving 300 R for lymphoid hyperplasia. Group II (308) had only a history of prior irradiation. Abnormal glands were found in 17 of 245 (7%) of Group I with 7 of 245 (3%) having nodular disease. No cancers were found in six of eight (75%) persons with nodular disease having surgery. Abnormal glands were found in 45/308 (14.6%) of Group II with 16/308 (5.2%) having nodular disease. Twelve of 16 (75%) with nodular disease from Group II had surgery and three thyroid cancers were found; in addition, one person from this group had a history of prior surgery for thyroid cancer. The incidence of thyroid cancer in Group I was 0%, Group II was 1.3%, and the combined incidence was 0.7%. The relatively low incidence of thyroid cancer observed is attributed to the relatively late average age at time of irradiation; 22 yr for Group I, 13 yr for Group II. (Author abstract) (13 Refs)

20. A RARE TYPE OF MULTIPLE ENDOCRINE NEOPLASIA: MEN IIB OR MEN III SYNDROME.

Chabloz R, Cavin R, Burckhardt P, Anani P, Saegesser F
Service de chirurgie A, CHUV, CH-1011 Lausanne, Switzerland
Schweiz Med Wochenschr; 112(24):842-852 1982

The MEN IIb syndrome is a rare form of multiple endocrine neoplasia, clearly defined more than 15 years ago, since which time more than 100 cases have been identified. It has a characteristic phenotype appearance which is unique and should permit more frequent diagnosis. The patient who is the subject of this study had passed through several different hospital departments without his very characteristic appearance being recognized or a diagnosis established. The marfanoid aspect of such patients is however very obvious, with kyphosis, skeletal asymmetry and funnel chest. The facial appearance of blunt features and thick lips is even more specific. The tongue and digestive mucosa are covered with small polypoid lesions which are submucosal ganglioneuromas. The visible presence of fine hyperplasic nerve fibers on the cornea is pathognomonic. This syndrome occurs sporadically but is generally transmitted genetically in an autosomal dominant manner. A medullary thyroid carcinoma, followed or preceded by pheochromocytoma (often bilateral), is associated with these dysmorphic signs. The tumors are themselves preceded by C-cell hyperplasia or adrenal medullary hyperplasia. The ganglioneuromas which predominate in the digestive tract exist from birth. The accompanying symptoms may, initially, be mistaken for inflammatory bowel disease. The prognosis is poor, since it relates to the evolution of the medullary thyroid carcinoma which is particularly malignant and presents at an early age. We have been following the course of this unusual disease of the APUD system in a young man, now aged 26 years, for over 2 years. (Author abstract) (45 Refs) (In FRE)

21. SIMULTANEOUS DETECTION OF THYROGLOBULIN (TG), THYROXINE (T4), AND TRIIODOTHYRONINE (T3) IN NONTOXIC THYROID TUMORS BY THE IMMUNOPEROXIDASE METHOD.

Kawaoi A, Okano T, Nemoto N, Shiina Y, Shikata T
Dept. Pathology, Yamanashi Medical Sch., 1110 Shimokato, Tamabo-mura, Nakakoma-gun, Yamanashi-ken 409-38, Japan
Am J Pathol; 108(1):39-49 1982

In 97 nontoxic thyroid tumors, detection of thyroxine (T4), and triiodothyronine (T3) was attempted by the immunoperoxidase method. T4 was demonstrated in 58 tumors (59.8%) and T3 in 76 (78.4%). The feasibility of biosynthesis of T4 and T3 by such tumors was thus established. In 65 of the tumors, we applied the immunostaining method to serial or semiserial sections to study the correlation among the localizations of thyroglobulin(Tg), T4, and T3. The localization of T4 agreed relatively well with that of Tg, and part of the Tg-positive structure frequently revealed simultaneous positive staining for T4. The localization of T3, however, did not always correspond with that of T4 or Tg. T4 and T3 with localizations identical to that of Tg may be considered to be bound to Tg, but the mode of existence of T3 without correspondence in localization to Tg remains unknown. (Author abstract) (34 Refs)

22. THE VALUE OF SERUM THYROGLOBULIN MEASUREMENT AS A MARKER OF CANCER RECURRENCE IN THE FOLLOW-UP OF PATIENTS PREVIOUSLY TREATED FOR DIFFERENTIATED THYROID TUMOR.

Roti E, Robuschi G, Emanuele R, Bandini P, Russo A, Riva P, Galassi E, Guerra UP, Manfredi A, Bozzetti A, Guazzi AM, Gnudi A
Cattedra di Endocrinologia e Patologia Costituzionale, Ospedali Riuniti, Via Gramsci 14, 43100 Parma, Italy
J Endocrinol Invest; 5(1):43-46 1982

The value of serum thyroglobulin (hTg) in detection of cancer recurrence was studied in 104 patients previously treated with surgical and 131I total thyroid ablation for differentiated thyroid cancer. In 87 of the patients with negative 131I total body scans (TBS), serum hTg was undetectable in 80%. In 57 patients with positive TBS, serum hTg was measurable in 72% of the patients, and undetectable in 20%. The results suggest that both serum hTg measurement and 131I TBS are useful in detection of thyroid cancer recurrence. (20 Refs)

23. NORMAL SERUM 1,25-DIHYDROXYVITAMIN D IN PATIENTS WITH MEDULLARY CARCINOMA OF THE THYROID.

Lee S, Morimoto S, Onishi T, Tsuji M, Okada Y, Seino Y, Ishida M, Yamaoka K, Takai S, Miyauchi A, Kumahara Y
Dept. Medicine and Geriatrics, Osaka Univ. Medical Sch., Fukushima-ku, Osaka, Japan
J Clin Endocrinol Metab; 55(2):361-363 1982

Serum calcium, phosphorus, calcitonin, parathyroid hormone, 25-hydroxyvitamin D (25OHD), and 1,25-dihydroxyvitamin D [1,25-(OH)2D] were measured in 6 women and 2 men with medullary carcinoma of the thyroid, 22 normal subjects, 5 patients with chronic renal failure, and 5 patients with primary hyperparathyroidism. Serum 1,25-(OH)2D levels were significantly higher in patients with primary hyperparathyroidism and lower in patients with chronic renal failure than in normal subjects. In patients with medullary carcinoma of the thyroid, the serum calcitonin levels were elevated, but the parathyroid hormone and 1,25-(OH)2D levels were within normal ranges. The serum 25OHD levels were not significantly different in any group. It is concluded that chronic elevation of serum calcitonin has no effect on the serum 1,25-(OH)2D level. (Author abstract) (18 Refs)

ADRENAL TUMORS

24. SCINTIGRAPHY IN PHEOCHROMOCYTOMA.

Winterberg B, Fischer M, Vetter H
(c/o Vetter) Med. Poliklinik, d. Universitat, Domagkstr. 3, D-4400 Munster, W. Germany
Klin Wochenschr; 60(12):631-633 1982

In four patients with pheochromocytoma, scintigraphy with 131I-meta-iodobenzylguanidine was performed to localize hyperfunctioning adrenergic tissue. In three patients unilateral adrenal pheochromocytoma was found, whereas one patient with a malignant pheochromocytoma showed multilocular dissemination. The results document that scintigraphy with 131I-meta-iodobenzylguanidine seems to be a safe and reliable method of detecting adrenal and extra-adrenal pheochromocytomas, both benign and malignant. (Author abstract) (3 Refs)

25. NONFUNCTIONING ADRENAL MASSES: INCIDENTAL DISCOVERY ON COMPUTED TOMOGRAPHY.

Glazer HS, Weyman PJ, Sagel SS, Levitt RG, McClennan BL
Mallinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, 510 S. Kingshighway, St. Louis, MO, 63110
AJR; 139(1):81-85 1982

Sixteen adrenal masses were identified with computed tomography (CT) in patients who had no clinical and biochemical evidence of adrenal pathology. In five patients, an adrenalectomy was performed, disclosing either an adenoma or nodular hyperplasia. Autopsy disclosed a cortical adenoma in one patient who died from unrelated causes. In the remaining 10 patients, follow-up scans 4-16 mo later revealed no change in the size of the masses. A management plan of nonfunctioning adrenal masses discovered incidentally on CT is proposed. (Author abstract) (26 Refs)

26. PRIMARY ALDOSTERONISM. TEN CASES OF SURGICALLY TREATED TUMORS.

Alexandre JH, Fraioli J, Boucherie J, Sage M, Regnard J
Clinique chirurgicale, Hopital Broussais, 96, rue Didot, 75674 Paris, France
Ann Chir; 36(5):363-367 1982

A series of 10 cases of primary aldosteronism caused by adrenal tumors is presented. Diagnosis was based on blood chemistry values, particularly low K values, and the presence of arterial hypertension. Computed tomography and isotope scanning were useful in localizing the lesions. In 8/10 cases the postoperative diagnosis based on histological examination of biopsy specimens was benign adenoma, and in 2/10 cases, the diagnosis was malignant adrenal adenoma. There was no mortality or morbidity associated with the procedures. (17 Refs) (In FRE)

27. PERSISTENT AND RECURRENT PHEOCHROMOCYTOMA: THE ROLE OF SURGERY.

Brennan MF, Keiser HR, Thompson NW
Gastric and Mixed Tumor Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
World J Surg; 6(4):397-402 1982

Eight patients (3 female, 5 male, 6-59 yr old) with persistent or recurrent pheochromocytoma were studied to validate localization procedures and document survival. Tumors were localized using computed tomography (CT) of the adrenals and lungs, iv pyelography, pulmonary tomography, chest x-ray, liver and bone scan, artertiography, ultrasonography, and selective venous sampling for catecholamines. Three patients had recurrent and five had persistent disease. Four patients had metastatic disease. Selective venous sampling for catecholamine levels accurately identified tumors in three patients: a local and systemic recurrence, a contralateral tumor, and an unsuspected lumbar primary. Adrenal CT scan was positive in all the three patients so studied. Ultrasound was not helpful in four patients. Two patients with metastatic disease underwent surgery directed not at ablating functional tumor but at resolving the complications of tissue destruction or obstruction by tumor masses. In patients with resectable disease, survival from diagnosis ranged from 1.5-15 yr. Patients with unresectable metastatic disease had survival ranging from 10-23 yr. Because long-term survival may occur following removal of both benign and malignant pheochrmocytomas, an aggressive surgical approach is recommended. (37 Refs)

28. A CASE OF PHEOCHROMOCYTOMA ORIGINATING FROM THE SUPERIOR CERVICAL SYMPATHETIC GANGLION.

Saito K, Sato O, Tsuruta J, Suematsu K
Dept. Neurosurgery, Sapporo Medical Coll., Hosp. S. I, W. 16, Sapporo 060, Japan
Neurol Med Chir (Tokyo); 22(2):154-158 1982

Pheochromocytomas are functionally active tumors which occur most commonly in the adrenal medulla but which can also develop in an extra-adrenal site. Over 90% of pheochromocytomas including extra-adrenal tumors are located between the diaphragm and the pelvic floor. Only two previous reports of pheochromocytoma originating from the cervical sympathetic chain were found in the literature. A third case of pheochromocytoma originating from the cervical sympathetic chain is presented. The patient was an 18-yr-old boy who was admitted to the Sapporo Medical College Hospital, because of attacks of palpitation, headache, generalized sweating and numbness in the four extremities during the past 3 yr. Paroxysmal hypertension was noted and a high level of noradrenalin in plasma and urine was shown. The patient was diagnosed as having a pheochromocytoma. However, it was difficult to detect the tumor. A tumor, which was situated on the right side of the neck at the angle of the jaw became enlarged and palpable after 1 yr. Selective angiography and CT were performed, and the tumor was removed. The tumor, which was 6 x 3.5 x 3.5 cm in size, had originated in the right superior cervical sympathetic ganglion. A pathological examination showed chromaffin paraganglioma or pheochromocytoma. The postoperative course was uneventful. (Author abstract) (21 Refs) (In JPN)

29. ADRENAL NEUROBLASTOMA SYMPATHICUM IN A 36-YEAR-OLD WOMAN.

van Berkel M, Van Rijn HJ, Lammers HA
Dr. A. Mathijsen Hosp., P. O. Box 90.000, Utrecht, The Netherlands
Eur J Nucl Med; 7(6):278-279 1982

The unexpected and initially unrecognized uptake of 99mTc-methylene diphosphonate on skeletal scintigraphy occurred in a 36-yr-old woman with adrenal neuroblastoma sympathicum. Diffuse increased tracer uptake was observed in the whole skeleton and in an area of marked irregularity superior to the left kidney. The left adrenal tumor and the left kidney were removed. Chemotherapy with adriamycin and cyclophosphamide was initiated. The patient developed spinal metastases and cranial nerve palsy and died after 20 mo of therapy. (2 Refs)

PANCREAS TUMORS

30. LOCALIZATION OF THE SOURCE OF HYPERINSULINISM: PERCUTANEOUS TRANSHEPATIC PORTAL AND PANCREATIC VEIN CATHETERIZATION WITH HORMONE ASSAY.

Cho KJ, Vinik AI, Thompson NW, Shields JJ, Porter DJ, Brady TM, Cadavid G, Fajans SS
Dept. Radiology, Univ. Michigan Medical Center, Ann Arbor, MI, 48109
AJR; 139(2):237-245 1982

Insulin concentrations were measured in the portal venous system through the percutaneous transhepatic approach in 12 patients with organic hyperinsulinism. Single insulinomas were found in 10, an adenoma and islet cell hyperplasia in one, and nesidioblastosis in one patient. Angiography localized adenomas in two. Local step-ups of insulin levels in the portal venous system, found in all patients with insulinomas, corresponded to tumor sites at surgery. Multiple step-ups were found in the portal venous system of the patient with nesidioblastosis and the patient with an adenoma with islet cell hyperplasia. Three tumors were localized in the head of the pancreas which would dictate the primary surgical approach rather than blind resection of the body and tail. Three of the 10 adenomas were not identifiable by palpation after pancreatic mobilization during surgery. In all patients, organic hyperinsulinism was cured after surgery. Percutaneous transhepatic portal and pancreatic vein catheterization with measurement of radioimmunoactive insulin concentrations is a safe and reliable method and may play an important role in the localization of adenomas in patients with normal angiographic studies and previous negative surgical explorations. (Author abstract) (16 Refs)

31. TOLBUTAMIDE AND SOMATOSTATIN TESTS IN THE DIAGNOSIS OF INSULINOMA.

Jara Albarran A, Caballero Asensi A, Garcia Peris P, Coste A, Toledano E, Gorospe C, Caviola E, Palacios Mateos JM
Servicio de Endocrinologia y Laboratorio de RIA, Hospital Oncologico, Madrid, Spain
Rev Clin Esp; 164(2):105-109 1982

Tolbutamide (Ta: 1 g iv) and Ta plus somatostatin (500 ug in a 60-min infusion) tests were performed in two patients with hypoglycemia due to insulinomas and in two with functional hypoglycemia. Somatostatin was found to inhibit the response to tolbutamide in the patients with functional hypoglycemia but not in those with insulinomas. This phenomenon disappeared after removal of the insulinomas. It is concluded that the tolbutamide-somatostatin test may be useful in the diagnosis of insulinoma when other diagnostic methods do not yield clear results. (16 Refs) (In SPA)

GONADAL TUMORS

32. TAMOXIFEN THERAPY FOR ADVANCED OVARIAN CANCER.

Schwartz PE, Keating G, MacLusky N, Naftolin F, Eisenfeld A
Dept. Obstetrics and Gynecology, Yale Univ. Sch. Medicine, 333 Cedar St., P.O. Box 3333, New Haven, CT, 06510
Obstet Gynecol; 59(5):583-588 1982

Thirteen patients with rapidly advancing recurrent epithelial ovarian cancers, in whom chemotherapy and, in some cases, radiation therapy failed, were treated with the estrogen antagonist tamoxifen. The presence of cytosol estrogen receptors, which have recently been identified in ovarian cancer specimens, was determined in the tumor from each patient prior to tamoxifen treatment. No complete responses were observed. One patient had a partial response and 4 patients had prolonged stabilization of disease. All patients with stabilized disease had estrogen receptor levels that were borderline or high. Eight patients demonstrated no response to oral tamoxifen therapy, but 5 of these had partial small bowel obstruction secondary to advanced recurrent cancer. As tamoxifen in this preliminary study may have stabilized rapidly advancing recurrent ovarian cancer, its role in the primary treatment of ovarian cancer in combination with cytotoxic chemotherapy should be considered. (Author abstract) (23 Refs)

33. IMMUNE HISTOCHEMICAL DEMONSTRATION OF TUMOR-ASSOCIATED ANTIGENS IN TESTICULAR GERM-CELL TUMORS.

Jacobsen GK, Jacobsen M, Clausen PP
Patologisk-anatomisk institut, Kobenhavns amts sygehus i Herley, DK-2730 Herlev, Denmark
Ugeskr Laeger; 144(18):1300-1303 1982

Fifty-eight consecutive testicular germ-cell tumors were investigated for the presence of alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) by the indirect immune peroxidase technique. Pure seminoma was diagnosed in 25/58 patients, embryonal carcinoma (EC) in 4, yolk sac tumor (YST) in 1, teratoma in 3, EC with seminomatous component in 5, EC with YST component in 1, EC with teratoma in 1, YST with teratomatous component in 2, EC with YST and teratomatous components in 6, YST with teratomatous and seminomatous components in 2, YST with choriocarcinoma in 2, EC with YST and seminomatous components in 3 and EC with YST, teratomatous and choriocarcinomatous components in 1. AFP was detected in 0/37 seminomatous components, 12/21 embryonal carcinoma components, 18/18 YST components, and 9/22 teratomatous components. HCG was detected in 3/3 choriocarcinoma components, 10/10 nonseminomatous components with syncytial giant cells, 1/1 seminoma with syncytial giant cells and 1/2 seminomas with tumor giant cells. No morphological difference was found between AFP-positive and AFP-negative embryonal carcinomas (AFP was present in 12/21 embryonal carcinomas). AFP was demonstrated in all types of yolk sac structures. HCG was demonstrated partly in the syncytiotrophoblasts of chorionic carcinoma components and in syncytial giant cells in 2 seminomas and 10 nonseminomatous tumors. Neither AFP nor HCG were demonstrated in the actual tumor tissue in seminomas or in components of seminomas. (9 Refs) (In DAN)

OTHER TUMORS OF GLANDULAR TISSUES

34. COMPARISON OF SURGICAL ADRENALECTOMY TO MEDICAL ADRENALECTOMY IN PATIENTS WITH METASTATIC CARCINOMA OF THE BREAST.

Wells SA, Worgul TJ, Samojlik E, Boucher AE, Lipton A, Harvey H, White D, Smart E, Cox C, Santen RJ
Dept. Surgery, Washington Univ. Sch. Medicine, 4960 Audubon Ave., St. Louis, MO, 63110
Cancer Res; 42(8,Suppl):3454s-3457s 1982

This study compared a form of 'medical adrenalectomy' with surgical adrenalectomy in a randomized, controlled trial. Ninety-six postmenopausal women with metastatic carcinoma of the breast were randomized to receive either surgical adrenalectomy or medical therapy po with an adrenal inhibitor, aminoglutethimide (AG) plus replacement hydrocortisone (HC). Forty medical patients and 29 surgical patients remained evaluable after inclusion into the study. None of the pretreatment variables differeed significantly between the groups of evaluable patients. Fifty-three percent of patients treated with AG plus HC had objective responses compared to 45% of patients treated by surgical adrenalectomy. An additional 5% in the surgical adrenalectomy category experienced disease stabilization. Regressions lasted 17.2 +-1.7 (S.E.) mo in the medical group and 17.1 +-2.2 in the surgical group. Median survival after objective response to AG plus HC did not differ significantly from that following surgery. Is surgical adrenalectomy superior to medical adrenalectomy? It was reasoned that AG plus HC would be preferred to surgical adrenalectomy on practical grounds if the operative method was not proved superior. The null hypothesis designed to answer this question was rejected. Therefore, the chance that surgical adrenalectomy is less than 1%. These data provide strong evidence that AG plus HC produces clinical remissions of breast carcinoma as frequently and for the same duration as does surgical adrenalectomy. (18 Refs)

35. TREATMENT OF ADVANCED BREAST CANCER WITH AMINOGLUTETHIMIDE: A 14-YEAR EXPERIENCE.

Gale KE
Upstate Medical Center, Syracuse, NY, 13210
Cancer Res; 42(8,Suppl):3389s-3396s 1982

Aminoglutethimide, derived from a nonbarbiturate soporific and originally introduced as an anticonvulsant drug, was subsequently discovered to inhibit steroid biosynthesis by interfering with the enzymatic conversion of cholesterol to delta(5)-pregnenolone. It has been found to interfere with the aromatization of androstenedione. This study is designed to exploit the hormone-manipulative property of aminoglutethimide in the treatment of advanced breast cancer. From July 1967 of July 1981, 91 women possessing histologically diagnosed symptomatic measurable advancing metastatic breast cancer refractory to current conventional therapy, including hormonal, were consecutively entered into the treatment study using aminoglutethimide with low-dose dexamethasone as a 'medical adrenalectomizer' in poor-risk patients. No patients possessed solely skin and soft tissue metastases. Preterminal patients were included in this study. Biochemical indices of adrenocortical and gonadal function were obtained pretreatment and periodically thereafter. Response criteria were established by the Eastern Cooperative Oncology Group. Patients with subjective and stabilization responses were considered nonresponders. Median survival time of responding patients was 22 mo, compared with 2 mo for nonresponding patients. Twenty-five of 73 patients with visceral dominant lesions responded. Initial patient performance status and dominant metastatic lesion were unrelated to response, but disease-free interval and site of relapse were related to drug toxicity. Treatment with aminoglutethimide provides effective palliation in poor-risk patients with advanced breast cancer with a response rate and survival time equal to those reported in better-risk patients following surgical adrenalectomy. (27 Refs)

36. AMINOGLUTETHIMIDE IN THE TREATMENT OF ADVANCED POSTMENOPAUSAL BREAST CANCER.

Harris AL, Powles TJ, Smith IE
Royal Marsden Hosp., Fulham Road, London SW3 6JJ, England
Cancer Res; 42(8,Suppl)::3405s-3408s 1982

A group of 213 unselected postmenopausal women with advanced breast cancer were treated with aminoglutethimide, 250 mg 4x a day, and hydrocortisone, 20 mg 2x a day. Follow-up is 10 mo to 4 yr from the start of treatment. In 190 assessable patients, there were 6 complete responses (CR), 47 partial responses (PR), 25 stable disease (SD), and 3 mixed responses. Overall objective response rate was 28% and with SD was 41%. Median duration of objective response was 14 mo. Objective response by site was: soft tissue, 31%; nodes, 27%; bone 23%; liver, 22%; and lung, 16%. A further 32% of patients with bone deposits had SD, and 19 of 60 patients with progressive disease had pain relief. Years after menopause, age and tumor-free interval did not affect response rates. Thirty-eight per cent of patients responding to previous endocrine therapy responded to aminoglutethimide compared with 19% of patients who had progressed on previous endocrine therapy. A group of 213 patients were assessable for toxicity. Main side effects were drowsiness (33%), rash (23%), and nausea (15%). Eleven patients stopped treatment because of toxicity. Median survival from start of treatment was 28 mo for PR-CR and for SD and 10 mo for progressive disease (p less than 0.001). Median survival from first metastasis was 43 mo for PR-CR, 40 mo for SD (not significantly different), and 22 mo for progressive disease (p less than 0.001). Aminoglutethimide is an effective endocrine therapy in advanced postmenopausal breast cancer, particularly for bone deposits. Disease stabilization is associated with symptomatic and survival benefit similar to CR-PR. (Author abstract) (22 Refs)

37. ADEQUACY OF ESTROGEN SUPPRESSION WITH AMINOGLUTETHIMIDE AND HYDROCORTISONE AS TREATMENT OF HUMAN BREAST CANCER: CORRELATION OF HORMONAL DATA WITH CLINICAL RESPONSES.

Santen RJ, Worgul TJ, Samojlik E, Boucher AE, Lipton A, Harvey H
Dept. Medicine, Div. Endocrinology and Oncology, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
Cancer Res; 42(8,Suppl):3397s-3401s 1982

Human breast neoplasms can be divided into hormone-dependent and hormone-independent subtypes. Estrogen is the major hormonal stimulus for growth of the dependent tumors. Failure to respond to estrogen suppression therapy could reflect either an incomplete lowering of estrogens or the hormonal independence of the tumor. We compared the levels of several estrogens and other hormones in women experiencing objective responses and disease progression during therapy with the aromatase-steroidogenesis inhibitor, aminoglutethimide, and replacement hydrocortisone. Pretreatment hormonal profiles of the estrogens, androgens, ketosteroids, thyroxine, polypeptide hormones, and carcinoembryonic antigen did not differ significantly among response groups. During treatment, the levels of all estrogens were suppressed to a similar degree in the progression group and in the responders. Data suggested that lack of estrogen suppression did not explain the response to treatment in the patients receiving aminoglutethimide-hydrocortisone. This finding differs from our results in a similarly analyzed control group of patients treated with surgical adrenalectomy. Levels of the weak androgens, dehydroepiandrosterone sulfate and androstenedione, were found to be higher in the progression group compared to the responders. This observation could not be explained by differences in duration of treatment between groups. Analysis at 1 to 12 wk, 13 to 24 wk, and 25 to 36 wk after initiating treatment indicated higher androgen levels at each time point in the progression group. While the finding of higher androgen levels in the responder group remains unexplained, this study indicates that incomplete estrogen suppression is not responsible for lack of tumor response in patients with progressive disease during aminoglutethimide-hydrocortisone therapy. (21 Refs)

38. USE OF AMINOGLUTETHIMIDE AS SECOND-LINE ENDOCRINE THERAPY IN METASTATIC BREAST CANCER.

Kaye SB, Woods RL, Fox RM, Coates AS, Tattersall MH
Dept. Oncology, Univ. Glasgow, Glasgow, Scutland
Cancer Res; 42(8,Suppl):3445s-3447s 1982

Sixty-five patients with advanced breast cancer, progressive despite prior endocrine therapy in all cases and prior chemotherapy in most cases, were treated with aminoglutethimide, 250 mg 4x a day. At present, 52 are evaluable for response assessment, and of these 10 (19%) showed an overall objective response, major sites of response being soft tissue and lung. A further 12 patients (23%) had stable disease during aminoglutethimide therapy while a total of 9 patients with bone metastases reported marked relief of pain without objective evidence of response. Forty-nine patients had received prior treatment with tamoxifen, and of the 10 tamoxifen responders 4 (40%) responded to subsequent aminoglutethimide, while of the 20 tamoxifen failures only 2 (10%) responded to subsequent aminoglutethimide. Aminoglutethimide was reasonably well tolerated, although six patients (9%) discontinued treatment because of intolerable side effects. Six of the 10 responding patients have subsequently relapsed, with a mean duration of response of 17 wk, but 4 continued to respond at 24, 32, 55, and 111 wk, respectively. The median survival from the start of aminoglutethimide therapy is in excess of 41 wk for responders and 11 wk for nonresponders, while the median survival from first relapse is 48 mo for aminoglutethimide responders and 28 mo for aminoglutethimide nonresponders. These results confirm that aminoglutethimide can offer a useful alternative form of endocrine therapy for advanced breast cancer, but the response rates obtained in heavily pretreated patients are inferior to those obtained when aminoglutethimide is used earlier in sequential treatment. For optimal results, particularly in terms of quality of life, aminoglutethimide should generally be used prior to chemotherapy. (Author abstract) (12 Refs)

39. AMINOGLUTETHIMIDE IN TAMOXIFEN-RESISTANT PATIENTS: THE MELBOURNE EXPERIENCE.

Murray RM, Pitt P
Endocrine Unit, Cancer Inst., Melbourne, Victoria, Australia
Cancer Res; 42(8,Suppl):3437s-3441s 1982

A group of 160 women with actively progressing metastatic breast cancer were treated with aminoglutethimide to induce medical adrenalectomy. The degree of adrenal suppression was monitored by measurement of dehydroepiandrosterone sulfate levels, and classification of response was carried out according to UICC criteria by two observers. Assessment of response is available for 136 patients, and of these 50 (36.7%) had an objective remission. In an additional 10 patients, the disease became static. Mean remission duration is 12.5 mo (range, 4 to 30). Forty-one patients had previously remitted to tamoxifen and then relapsed, and of these 22 (53.6%) experienced another remission with aminoglutethimide. Fifty patients had failed to respond to tamoxifen, and of these 16 (32%) had a remission with aminoglutethimide. In the 20 patients who did not receive tamoxifen and in the 25 whose response to it could not be classified, the remission rates to aminoglutethimide were 25 and 28%, respectively. The high remission rate to medical adrenalectomy in patients who have previously responded to tamoxifen makes it the treatment of choice in tamoxifen-responsive patients. (Author abstract) (6 Refs)

40. TAMOXIFEN AND AMINOGLUTETHIMIDE IN ADVANCED BREAST CANCER.

Corkery J, Leonard RC, Henderson IC, Gelman RS, Hourihan J, Ascoli DM, Salhanick HA
New England Deaconness Hosp., Boston, MA, 02115
Cancer Res; 42(8,Suppl):3409s-3414s 1982

Tamoxifen (TAM), a standard endocrine treatment for advanced breast cancer, probably acts by competing for the estrogen receptor protein in the breast tumor cells. If so, resistance to TAM may be a function of the level of the available endogenous estrogen. Inhibition of estrogen synthesis by aminoglutethimide may therefore facilitate the action of the antiestrogen. To test this hypothesis, the two agents were given concurrently (a) to patients who had become resistant to TAM and (b) to patients who had never received TAM in a randomized cross-over study against TAM alone. Patients with estrogen receptor protein-negative disease were excluded. Estrogen and aminoglutethimide levels were measured serially. In the first study, 4 of 26 patients experienced partial responses, and 4 of 26,, stabilization of their disease. In the randomized study, 4 of 11 patients on the combination and 3 of 9 of TAM alone had responses. Two patients on the combination and three on TAM alone had stabilization of disease. In the first group, the low rate of response may be attributed to extensive prior treatment. In the randomized study, there is presently no clear advantage for one treatment, and overall, there was no statistically significant correlation between degree of estrogen suppression, aminoglutethimide level, and response. The findings do not exclude the possibility that these agents may act in breast cancer by mechanisms other than inhibition of estrogen receptor. (Author abstract) (23 Refs)

41. TRIAL OF TAMOXIFEN AT A DOSE OF 40 MG DAILY AFTER DISEASE PROGRESSION DURING TAMOXIFEN THERAPY AT A DOSE OF 20 MG DAILY.

Stewart JF, Minton MJ, Rubens RD
Imperial Cancer Res. Fund, Breast Cancer Unit, Guy's Hosp., London SE1 9RT, England
Cancer Treat Rep; 66(6):1445-1446 1982

A prospective nonrandomized trial was conducted in 36 consecutive patients (av age 64.9 yr) to assess the response of advanced breast cancer to 20 mg tamoxifen (TO) bid after disease progression during therapy with 10 mg bid. The patients studied had histologically confirmed, locally advanced inoperable or metastatic breast cancer that was progressing during treatment with 10 mg TO bid with or without 5 mg prednisone (PR) bid. Characteristics of the 30 evaluable patients are presented. No objective responses to the higher dose of TO were observed. Seven patients had stable disease for 2-15 mo, two who had responded to previous endocrine therapy (TO, PR), and five who had had no prior response. These patients comprised two with estrogen receptor (ER)-positive (greater than or equal to 5 femtomole; fmol/mg of cytosol protein) tumors, one with ER-negative (less than 5 fmol/mg of cytosol protein) tumor, and four with unknown ER tumor status. The other 23 patients all had progressive disease. Median time to treatment failure was 2 mo (range 1-15 mo), and median survival from study entry was 11 mo (range 2-17 mo). Results indicated that escalation of TO dosage to 20 mg bid after disease progression during therapy with 10 mg bid does not lead to further response and that alternative therapy, either endocrine or cytotoxic, should be given. (5 Refs)

42. ANTIESTROGEN TREATMENT OF BREAST CANCER: AN OVERVIEW.

Pearson OH, Manni A, Arafah BM
Dept. Medicine, Case Western Reserve Univ. Sch. Medicine, Univ. Hosp., Cleveland, OH, 44106
Cancer Res; 42(8,Suppl):3424s-3429s 1982

Tamoxifen has emerged as a highly effective, nontoxic endocrine therapy for women with Stage IV and II estrogen receptor-positive breast cancer. Tamoxifen appears to act by blocking endogenous estrogen action at the target tissue level rather than by suppression of circulating estrogen levels. In a series of 113 consecutive, selected patients with Stage IV breast cancer, tamoxifen induced objective remissions in 50%. Recent randomized studies comparing pharmacological doses of estrogen vs tamoxifen in postmenopausal women with Stage IV breast cancer have shown comparable results with these two modalities. Antiestrogen therapy has been shown to be effective in some patients after prior endocrine additive therapy and, in particular, after ablative procedures, such as ovariectomy, adrenalectomy, and hypophysectomy. It has been shown that circulating estrogens are not completely eliminated following ablation of these endocrine glands, which may account for the effectiveness of antiestrogen in this setting. Other endocrine therapies have been shown to be effective after prior treatment with antiestrogen. Recent studies have shown that aminoglutethimide plus hydrocortisone may also induce remissions in some patients after prior treatment with tamoxifen. This latter finding is of particular interest since aminoglutethimide is thought to work by blocking estrogen production, and the finding suggests that tamoxifen does not completely block all endogenous estrogen activity. Fluoxymesterone has been shown to induce remissions after tamoxifen or after tamoxifen plus hypophysectomy, and there was no correlation between the response to antiestrogen and subsequent response to androgen. Because of its effectiveness and minimal side effects, tamoxifen is considered to be an initial endocrine therapy of choice in women with breast cancer. However, it has its limitations, as demonstrated by the results of secondary endocrine therapies such as hypophysectomy, medical adrenalectomy, and androgen therapy. (28 Refs)

43. RELATIONSHIP OF OBESITY TO BLOOD ESTROGENS.

Zumoff B
Div. Endocrinology and Metabolism, Dept. Medicine, Beth Israel Medical Center, New York, NY, 10003
Cancer Res; 42(8,Suppl):3289s-3294s 1982

It has become conventional wisdom that estrogenic stimulation of breast tissue has something to do with the causation of breast cancer and that the reason obesity is a risk factor for breast cancer is that obese women are hyperestrogenized. However, it has been very difficult to demonstrate that excessive exogenous estrogen increases the incidence of breast cancer, that endogenous estrogen excess is present in breast cancer, or that obese women are hyperestrogenized. We have examined the last question by measuring 24-hr mean plasma estrone and estradiol levels in the midfollicular phase in 18 healthy, regularly cycling, very obese (53 to 218% above ideal weight) women and 16 regularly cycling, age matched, nonobese control women. Unlike obese men, the obese women showed no significant elevation of either estrone or estradiol. Their av estrone level was 72 compared with 64 pg/ml in controls; their average estradiol level was 65 compared with 57 pg/ml in controls. In the combined group (obese plus nonobese), there was a significant correlation of percentage of deviation from ideal weight with plasma estrone ($y = 63 + 0.12x$; p less than 0.05) but not with estradiol. This correlation supports the current hypothesis that there is increased androstenedione/estrone conversion (ie, increased aromatase activity) in obesity. The reason plasma estrone levels are not significantly elevated in obese women is that the small amount derived from androstenedione is swamped by the much larger amount derived from ovarian secretion, which is apparently unaffected by obesity. Unless there is increased local formation of estrogens in the breast tissue of obese women, the absence of elevated plasma estrogens in them means that their breasts are not 'seeing' increased estrogen levels. Thus, endogenous hyperestrogenization is unlikely to be a causative factor of breast cancer in obese women. (Author abstract) (48 Refs)

44. REVIEW: ORAL CONTRACEPTIVES AND MENOPAUSAL ESTROGENS IN RELATION TO BREAST NEOPLASIA.

Brzezinski A, Schenker JG
Dept. Obstetrics and Gynecology, Hadassah Univ. Hosp., POB 12000, 91120 Jerusalem, Israel
Isr J Med Sci; 18(4):433-438 1982

The possible association of oral contraceptives (OC) and menopausal estrogens (ME) on development of breast cancer is reviewed. The high incidence of breast cancer concurrent with extensive OC-ME usage, considered together with the relatively high hormone dependence of breast tumors and the placement of the breast as a target organ in the estrogen-progesterone hormonal pathways supports this association. Theories of the hormonal etiology involve estriol, progesterone, androgens, and the pineal gland; however, the specific hormonal etiology is unclear. Most studies have demonstrated significantly decreased risk of benign breast disease in women using OC. Since increased parity and early first birth are potentially protective conditions for breast cancer, OC, by simulating pregnancy, may exert a protective effect. The incidence of benign breast disease appears to be inversely related to the amount of progesterone in different OC. No significant overall increase in the risk of breast cancer has been demonstrated among users of OC. However, specific subgroups in which an increased risk was shown have been identified, including women with previous biopsy of benign breast disease. Evidence is available associating ME with an increased risk of endometrial carcinoma. Recent studies have demonstrated a positive association between ME and breast cancer. Caution is suggested in long-term use of OC and the continuous use of ME for periods greater than 10 yr should be reconsidered. (57 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

45. GONADAL FUNCTION AFTER COMBINATION CHEMOTHERAPY FOR HODGKIN'S DISEASE IN CHILDHOOD.

Whitehead E, Shalet SM, Morris Jones PH, Beardwell CG, Deakin DP
(c/o Shalet), Christie Hosp. and Holt Radium Inst., Wilmslow Road, Manchester M20 9BX, England
Arch Dis Child; 57(4):287-291 1982

The effect of quadruple chemotherapy (mustine, vincristine, procarbazine and prednisolone) on gonadal function was investigated in 15 males and 2 females treated for Hodgkin's disease during childhood. The two females have regular menstrual cycles with evidence of ovulation in one. Twelve of the males have shown normal progression of pubertal development since completing their treatment. Nine out of 10 late pubertal or adult subjects had small testes but only one developed gynecomastia. All four prepubertal subjects had normal basal and peak gonadotrophin responses to luteinizing hormone-releasing hormone. Nine of the 12 subjects studied during puberty or adulthood had either an increased basal serum follicle-stimulating hormone (FSH) level or an exaggerated FSH response to luteinizing hormone-releasing hormone. Each of the six males who provided semen for analysis was azoospermic after an interval of between 2.4 and 8 (mean 5.3) yr after completion of treatment. We conclude that severe testicular damage is common after treatment with mustine, vincristine, procarbazine, and prednisolone in childhood. The germinal epithelium is particularly vulnerable and the resultant azoospermia is likely to be irreversible. The Leydig cells are less susceptible to cytotoxic-induced damage. Pubertal development is normal and there is no indication for androgen replacement therapy. (Author abstract) (20 Refs)

46. ENDOCRINE COMPLICATIONS OF RADIOTHERAPY IN THE CHILD.

Lucas C, Garnier J

Travail du Service de Pediatrie et Genetique Medicale, Hopital d'Enfants C.H.U. de la Timone, 13385 Marseille, France

Pediatrie; 37(2):157-160 1982

The pituitary and thyroid gland are affected by radiotherapy even when the malignant tumor is not directly next to the gland. This is the case with cerebral tumors, all extracranial irradiated tumors of the head and neck, and cancers of the CNS or bone marrow. Radiation induced deficits of the pituitary may lead to growth and maturation problems. Ionizing radiation may lead to secondary, induced cancer of the thyroid. The risk of thyroid cancer is greatest in younger children exposed to radiation in therapeutic doses. (16 Refs) (In FRE)

47. BIOCHEMISTRY OF AROMATASE: SIGNIFICANCE TO FEMALE REPRODUCTIVE PHYSIOLOGY.

Ryan KJ

Lab. Human Reproduction and Reproductive Biology, Harvard Medical Sch., Boston, MA, 02115

Cancer Res; 42(8,Suppl):3342s-3344s 1982

The formation of estrogens in mammals via aromatase involves the relatively unique capacity to form an aromatic ring de novo in contrast to most other aromatic substances (essential amino acids) which are obtained only in the diet. The reaction is the only example of a cytochrome P-450 system which resides in both the mitochondrial and microsomal fractions of the cell. It occurs widely throughout the body in diverse tissues and functions via both de novo synthesis and transformation of prehormones (androstenedione and testosterone). It is found widely in animal species in both the brain and gonads even in phylogenetically primitive species. Placental aromatase appears to be associated with the evolution of viviparity and an extended gestational period in utero. Follicular aromatase which is dependent upon follicle-stimulating hormone stimulation appears to be essential for oogenesis, ovulation, and normal luteal functions while central nervous system aromatase serves to determine sexual behavior and the neurohormonal link to the hypothalamus and pituitary for ovarian cyclicity. While estrogens are the key to pituitary, breast, and endometrial growth and development, this hormone is one of the few examples of an endogenous steroid that has been implicated as a carcinogen or a stimulant for carcinogenesis. (Author abstract) (18 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

48. DOES THE ECTOPIC SECRETION OF ACTH EXIST?.

Vereshchagina GV
Res. Inst. Biological Testing of Chemical Compounds, Kupavna, USSR
Eksp Onkol; 4(3):11-19 1982

Incidence of various hormonal disorders in cancer patients is reviewed, with special emphasis on the ectopic production of ACTH. The criteria of ectopic ACTH syndrome include correlation between increased blood level of ACTH and growth of tumor; absence of direct involvement of adrenals or hypothalamo-pituitary region; presence of ACTH in the tumor tissue; arterio-venous gradient of ACTH concentration; ability of tumor cells to produce ACTH in vitro; changes in functional state of ACTH-secreting endocrine glands; and persistence of elevated ACTH concentration following removal of ACTH-secreting endocrine glands. (91 Refs) (In RUS)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

49. THYROTROPIN RELEASING HORMONE RECEPTORS IN REGULATION OF PROLACTIN GENE EXPRESSION IN GH CELLS.

Mu MC, Chakrabarti S, Hanes SD, Biswas DR
(c/o Biswas) Lab. Pharmacology, Harvard School Dental Medicine, Boston, MA, 02115
Biochem Biophys Res Commun; 106(3):811-817 1982

The thyrotropin releasing hormone (TRH) receptor-modulated regulation of prolactin (PRL) gene expression was studied in three GH cell strains (rat pituitary tumor cells in culture). The three strains synthesize different amounts of PRL and exhibit different responses to TRH. Binding affinities and the number of receptors/cell were studied and the effect of epidermal growth factor on PRL gene expression in the different cell strains was explored. One strain (GH4C1) responded to TRH by stimulating PRL production while the hybrid strain (928-9b) and the bromodeoxyuridine-resistant strain (F1BGH12C1) did not. When binding of 3H-TRH was studied as a function of TRH concentration, the affinities of TRH to its specific receptors were similar in both GH4C1 and 928-9b cells. However, the number of TRH receptors/cell was significantly different in the two strains; GH4C1 cells had a max number of specific binding sites of 1.05 x 10(5)/cell, while 928-9b cells had a max number of 0.16 x 10(5)/cell. Thus, in the two strains, the TRH-responsive GH4C1 cells and the TRH-nonresponsive cells, the total number of TRH binding sites per cell was much less in the TRH-nonresponsive cell line. The inadequate number of TRH receptors in 928-9b cells may be responsible for the nonresponsive property of the hybrid cells to TRH and a possible role of the number of specific receptors in the regulation of the peptide hormone action is suggested. (11 Refs)

50. CYTOLOGICAL STUDY ON THE ANTERIOR PITUITARY OF SENILE UNTREATED BEAGLE BITCHES WITH SPONTANEOUS MAMMARY TUMOURS.

Attia MA
Drug Safety R and D Lab., Organon International B.V., P.O. Box 20, Oss, The Netherlands
Arch Toxicol; 50(1):35-45 1982

Pituitaries were obtained from senile untreated Beagle bitches of comparable age (7-9 yr) and genital status. The animals were divided into three groups; one was normal (without mammary lesions), one had benign tumors and one had mammary adenocarcinomas. PRL-, STH-, ACTH- and gonadotrophin-producing cells are studied and counted in serial paraffin sections stained with histochemical techniques. The animals with mammary malignancy displayed a marked increase in the relative number of PRL and ACTH cells with morphological signs of higher secretory activity in most cells, compared with that in normal bitches or bitches with benign tumors. STH cells in bitches with adenocarcinomas were reduced in number; however the secretory activity in these animals was the same as that observed in the normal bitches. In the animals with benign mammary tumors, STH cells showed morphological indication of higher secretory activity than in the other groups. PRL and ACTH cells were slightly increased in number and had slightly higher activity than that in normal bitches. These findings may suggest a role for hypophyseal hormones in mammary neoplasias. (Author abstract) (18 Refs)

51. ALTERNATIVE RNA PROCESSING IN CALCITONIN GENE EXPRESSION GENERATES MRNAS ENCODING DIFFERENT POLYPEPTIDE PRODUCTS.

Amara SG, Jonas V, Rosenfeld MG, Ong ES, Evans RM
Div. Endocrinology, Sch. Medicine, Univ. California, San Diego, La Jolla, CA, 92093
Nature; 298(5871):240-244 1982

Alternative processing of RNA transcripts from the calcitonin gene results in the production of distinct mRNAs encoding the hormone calcitonin or a predicted product referred to as calcitonin gene-related peptide (CGRP). The calcitonin mRNA predominates in the thyroid while the CGRP-specific mRNA appears to predominate in the hypothalamus. These observations lead us to propose a model in which developmental regulation of RNA processing is used to increase the diversity of neuroendocrine gene expression. (Author abstract) (34 Refs)

52. EXPERIMENTAL TUMORS FROM C-CELLS OF THE THYROID GLAND.

Fedchenko NP
Medical Inst., Dnepropetrovsk, USSR
Eksp Onkol; 4(3):34-37 1982

Effect of prolonged hypercalcemia on morphology of C-cells of the thyroid gland was studied in random-bred male rats subjected to administration of calcium chloride in combination with vitamin D2 (1,000 IU/ml). After 12-mo exposure, the rats were sacrificed, and the histology of the thyroid gland was evaluated. The hypercalcemia that was induced brought about a progressive increase in the number of C-cells. This proliferation of C-cells was associated with intensive formation of new follicles. The parenchyma of the thyroid gland was divided into two zones. The central zone was characterized by the presence of small follicles and a large number of C-cells. The peripheral zone was characterized by larger follicles and an absence of C-cells. The size of follicular thyrocytes in the hypercalcemic rats did not differ from that in control rats. The number of follicles in the hypercalcemic rats was 133% greater than that in the controls. The proliferation of C-cells led to adenomas in 28% of the animals. (6 Refs) (In RUS)

53. ESTROGEN SYNTHESIS IN HUMAN BREAST TUMOR AND ITS INHIBITION BY TESTOLOLACTONE AND BROMOANDROSTENEDIONE.

Dao TL
Dept. Breast Surgery and Breast Cancer Res. Unit., Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(8,Suppl):3338s-3341s 1982

A total of 53 tumors have been examined for estrogen synthesis from androstenedione and assayed for estradiol receptors. It was found that of the 40 tumors that metabolized androstenedione to estrogens, 17 tumors were estradiol receptor negative and 23 tumors were estradiol receptor positive. Of the 13 tumors that did not synthesize estrogens, 7 tumors were receptor negative and 6 tumors were receptor positive. No correlation was found between the ability of the tumor to synthesize estrogens and the presence or absence of estradiol receptors. The inhibition of aromatase enzyme in human breast tumors by delta(1)-testololactone, testololactone, and 6alpha-bromoandrostenedione and 6beta-bromoandrostenedione was investigated. Estrone and estradiol synthesis from androstenedione was reduced in five tumor incubations by the presence of 0.2 mM delta(1)-testololactone and testololactone. 6alpha- and 6beta-bromoandrostenedione (2.0 uM) were also shown to block estrogen synthesis in five tumors. Furthermore, Lineweaver-Burk plots revealed that all four compounds were competitive inhibitors of androstenedione aromatization. An apparent Km of the aromatase enzyme for androstenedione of 0.08 uM and a Vmax of 23 pmol of estrone synthesized per g tumor per hr were determined for one human breast tumor specimen. The use of an aromatase inhibitor such as delta(1)-testololactone in the treatment of breast cancer should be reconsidered. Data from one patient with advanced cancer of the breast, responding to previous oophorectomy and adrenalectomy and treated with large doses of delta(1)-testololactone, are presented to illustrate the significance of successful treatment by scientific approaches. (Author abstract) (25 Refs)

54. ENHANCED AND REVERSED GROWTH IN VIVO OF A PREGNANCY-DEPENDENT MOUSE MAMMARY TUMOR (TPDMT-4) BY A GONADOTROPIN-RELEASING HORMONE AGONIST ANALOG.

Matsuzawa A, Yamamoto T
Lab. Animal Res. Center, Inst. Medical Science, Univ. Tokyo, P.O. Takanawa, Tokyo 108, Japan
Eur J Cancer Clin Oncol; 18(5):495-505 1982

TPDMT-4 pregnancy-dependent mammary tumors grow continuously in DDD female mice carrying pituitary isografts (PI) ectopically or bearing an sc 17beta-estradiol plus progesterone (EP) pellet. A gonadotropin-releasing hormone (GnRH) agonist (D-leucyl6, des-glycyl-NH210, prolyl-ethylamide9) GnRH (TAP-144), was examined for its antitumor activity in these experimental systems. TAP-144 was injected ip at doses of 300 and 600 ug 6x weekly, when tumors grew to significant sizes. TAP-144 enhanced tumor growth during the first 2 weeks and subsequently reversed it in a dose-related manner in PI-bearing mice. The agonist did not affect tumor growth in the absence of ovaries in these mice. In ovariectomized mice, TAP-144 enhanced EP pellet-induced tumor growth but never reversed it. In ovariectomized, PI-bearing mice. TAP-144 first enhanced and subsequently reversed tumor regrowth induced by ovarian grafts to a greater extent when commencing it simultaneously with ovarian grafting than 30 days before it. The agonist also exerted the dual effects on TPDMT-4V ovarian-dependent subline tumors in the absence of PI. In TAP-144-treated mice, enhanced tumor growth was related to many solid corpora lutea in ovaries and fully developed mammary glands, but reversed growth was related to atrophied luteal components and mammary glands. The results suggest that TAP-144 enhances tumor growth first via its stimulative action on the pituitary-ovarian axis and causes tumor regression later via its direct inhibitory action on ovaries. (Author abstract) (31 Refs)

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PITUITARY, HYPOPHYSEAL, AND PINEAL TUMORS

1. PHLEBOGRAPHY OF THE CAVERNOUS AND INTRACAVERNOUS SINUSES; AN INVESTIGATION COMPLEMENTARY TO COMPUTED TOMOGRAPHY (CT) IN THE DETECTION OF INTRASELLAR SPACE-OCCUPYING LESIONS.

Smaltino F, Iaccarino V, De Divittiis E, Cirillo S, Elefante R, Spaziante R

Istituto di Radiologia, II Facolta di Medicina e chirurgia dell'Universita, Via Pansini, 5, 80131 Naples, Italy

Radiol Med (Torino); 68(7/8):565-569 1982

Two patients with craniopharyngiomas, three with invasive chromophobic adenomas, six with empty sella, and nine with suspected pituitary microadenomas were subjected to perihypophyseal phlebographic examinations. Microadenoma, confirmed surgically, was demonstrated in 6/9 patients in whom the CT findings were inconclusive or negative. Adenoma was found in 3/6 patients with empty sella. Perihypophyseal phlebography is valuable as a method complementary to CT in the

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diagnosis of microadenomas and of pituitary tumors in empty sella. (20 Refs) (In ITA)

2. THE EMPTY SELLA AND PITUITARY ADENOMAS: A THEORY ON THE CAUSAL RELATIONSHIP.

Bjerre P, Gyldensted C, Riishede J, Lindholm J

Dept. Neurosurgery, Div. Neuroendocrinology, NK 2091, Rigshospitalet, DK-2100 Copenhagen, Denmark

Acta Neurol Scand; 66(1):82-92 1982

Enlargement of the sella was studied in 44 patients by computed tomography (CT) with air contrast enhancement. Solid tumors were found in 24 patients. The sella was completely or partially empty in 20 patients (9 men, 24-69 yr old, median 50 yr; 11 women 27-66 yr old, median 33 yr). CT indicated water absorption values for the entire sella in 4 patients and part of the sella in 16 patients. Intrasellar enhancement was observed in 13/16 patients with partially empty sellas. Ten patients had had previous acute episodes with signs and symptoms including headache, nausea, vomiting, mental confusion, impaired consciousness, hemiparesis, hemiparesthesia, ophthalmoplegia, fever, and stiff neck. The median age was 48 yr for seven men and three women with such episodes and 33 yr for two men and eight women without such episodes. Eight patients had unilateral sellar ballooning, bony destruction, or both . In six of these patients CT indicated the corresponding portion of the sella was empty. Contrast studies in seven patients produced normal findings in three and showed intrasellar cisternal herniation in four. Findings in patients with empty sellas are consistent with the hypothesis that empty sella may result from an infarction involving all or part of a pituitary adenoma. The infarction may or may not cause neurological symptoms. Late effects may include rhinorrhea or hydrocephalus. (37 Refs)

3. RADIOLOGIC DETECTION OF SECRETING PITUITARY ADENOMAS.

Metzger J, Gardeur D, Thibierge M, Pehuet M, Poirier M

Service de Neuro-Radiologie, Hopital de la Pitie, 83, boulevard de l'Hopital, F 76551 Paris, France

Ann Med Interne (Paris); 133(1):6-11 1982

Secreting pituitary adenomas which are small and barely symptomatic are often detected by radiographic exploration of the sella turcica. Useful examinations include standard radiographs computed tomography (CT) analysis, and in certain exceptional cases, gas encephalography and even arteriography. Enlargement in the volume of the sella turcica is a classic sign of pituitary adenoma, but since it is a late appearing sign, other, less obvious signs must be sought. Radiologic modifications that are related to adenomas are often localized either medially or laterally and with an anterior-inferior or posterior-inferior development. CT is superior to standard radiographs because both the contents and the structure of the sella turcica can be visualized. CT diagnosis of small intrasellar adenomas is of variable difficulty depending on tumor volume, site, and density following iv injection of the contrast material. In all cases, a diagnosis will depend on the confrontation of indirect and direct signs. Encephalography is necessary when a distinction must be made between a hypodense pituitary adenoma and an empty sella turcica. Arteriography should be performed when symptomatology is atypical and when vascular malformations or a meningioma of the cavernous sinus are suspected. (no Refs) (In FRE)

4. SPARSELY GRANULATED PROLACTIN CELL ADENOMAS OF THE PITUITARY GLAND. CORRELATION OF ULTRASTRUCTURE WITH PLASMA HORMONE LEVEL.

Dingemans KP, Assies J, Jansen N, Diegenbach PC
Dept. Pathology, Univ. Amsterdam, Wilhelmina Gasthuis, Eerste Helmersstraat 104, NL-1054 EG Amsterdam, The Netherlands
Virchows Arch [Pathol Anat]; 396(2):167-186 1982

The possible relationship between the preoperative plasma prolactin levels of patients having a sparsely granulated prolactin cell adenoma of the pituitary gland and the morphology of the tumors was studied by means of quantitative electron microscopy. To this end, a number of ultrastructural variables were chosen which are generally regarded to be indicative of cellular activity and which could be determined in a quantitative or semiquantitative way. These variables were determined in 19 adenomas from 17 patients and plotted against the corresponding prolactin levels. It appeared that marked endocrine activity was associated with a small number of granules per cell, a high frequency of exocytosis, and a marked development of the rough endoplasmic reticulum. Granule size and development of Golgi apparatus and lysosomes were not at all, or only poorly correlated with the plasma hormone levels. Finally, the number of mitochondria per cell showed a totally unexpected inverse correlation with endocrine activity. Due to the close mutual correlation existing between several of the variables investigated, combining them in a multivariate analysis did not significantly improve the correlation with the hormone level. (Author abstract) (49 Refs)

5. A LIGHT AND ELECTRON MICROSCOPIC STUDY OF ADENOCARCINOMA OF THE PITUITARY GLAND.

Zhang F
Dept. Neurologic Pathology, Inst. Neurology, Shanghai First Medical Coll., Shanghai, People's Republic of China
Zhonghua Shenjing Jingshenke Zazhi; 14(4):210-212 1981

Light and electron microscopic studies were made on a surgical specimen from a 26-yr-old female who received surgeries to remove brain tumors. The light microscope showed that the tumor tissue was rich in blood vessels, and tumor cells grew along capillary and fibrous tissue to make the papillary form. Nuclei were either at the center or toward capillaries. In the electron microscope, the tumor cell showed nest-like or papillary distribution with flat cell to cell contact. Nuclei were large, full of chromosomes, with relatively less cytoplasm. Two kinds of secreted granules were seen, a black, iron-binding one and a light gray, less iron-binding granule. The findings suggest that the tumor is probably derived from a less differentiated chromophobe. (11 Refs) (In CHI)

6. PROLACTIN SECRETING PITUITARY ADENOMAS. EXPLORATIONS AND TREATMENT.

McGregor A, Scanlon M, Hall R
Dept Medicine, Welsh National School Medicine, Heath Park, Cardiff, Wales CF 44 XN, England
Ann Med Interne (Paris); 133(1):51-57 1982

Prolactin secreting adenomas (PSA) account for 32% of secreting pituitary adenomas. Better understanding of the neuroendocrine control of prolactin secretion has permitted earlier diagnosis of PSA. Hormone testing and radiographs are essential elements in establishing a diagnosis of PSA. Although the existence of an abnormal sella does not exclude another pathology, the most probable cause is an expansive pituitary adenoma. Elevated basal levels of prolactin are not sufficient proof of an adenoma and exaggerated response of thyroid stimulating hormone to hormone challenge may be useful in diagnosing such lesions. The three therapeutic modalities which are available to treat pituitary adenomas are surgery, radiotherapy, and chemotherapy. The most encouraging surgical studies have reported prolactin normalization in 70% of patients. Bromocriptine has been shown to inhibit prolactin secretion and tumor growth during the time when it is taken. Reduction in the size of the prolactin macroadenomas has been associated with the disappearance of symptoms and an improvement in pituitary function. (28 Refs) (In FRE)

7. PITUITARY PROLACTINOMAS.

Nabarro JD
Middlesex Hosp., London W1N 8AA, England
Clin Endocrinol (Oxf); 17(2):129-155 1982

A distinction is made between large and small prolactinomas. They have different presenting symptoms, sex distribution and natural history. From a series of 263 patients with obviously enlarged pituitary fossae on lateral skull x-ray, 74 were identified as having chromophobe adenomas and 34 of these are believed to have prolactinomas. A modestly elevated prolactin level with an enlarged pituitary fossa does not mean that the patient has a prolactinoma, the hyperprolactinemia may be due to interference with the hypothalamic prolactin inhibiting mechanism. The special problems of acromegaly are discussed. The presenting symptoms and sex incidence are reviewed. Review of 48 cases of large prolactinoma shows that it may be an unpleasant invasive tumor. Treatment by transfrontal or transphenoidal surgery occasionally results in a cure but are generally disappointing. X-ray therapy is relatively ineffective. Bromocriptine may produce dramatic response but occasional cases are resistant to its action. The value of serial prolactin measurements to monitor tumor growth is stressed. The results of transsphenoidal surgery in 36 patients with higher prolactin levels are reported. The natural history of the small prolactinoma is discussed, the reported incidence of small prolactinomas at autopsy is noted. The advice to be given to a patient with a small prolactinoma who wishes to get pregnant is reviewed. It is suggested that special care should be exercised if the prolactin level exceeds 4,000 mU/l. The floor of the pituitary fossa should be scrutinized on tomograms and the upper limit by computerized tomography. If close observation of the patient is possible through pregnancy, bromocriptine may be given to restore ovulation. If the prolactin level rises excessively or a visual field defect occurs, bromocriptine should be restarted at once. The effect of x-ray therapy on prolactin levels in 15 patients is reported. High prolactin levels are little changed, four patients with lower initial levels achieved normoprolactinemia in 2-6 yr. (50 Refs)

8. PROGRESS IN THE HORMONAL DETECTION OF PROLACTIN ADENOMAS.

De Gennes JL, Turpin G, Hesmati H, Carayon A
Service d'endocrinologie Metabolisme, Hopital de la Pitie, Paris, France
Ann Med Interne (Paris); 133(1):12-16 1982

The prolactin hormonal profiles of 13 normal subjects (Group A) were compared with those of 25 patients with radiologically evident pituitary adenomas (Group B), with 13 hyperprolactinemic patients without radiologic signs of an adenoma (Group C), and with 12 patients with secondary hyperprolactinemia (Group D). In Group B, the fasting prolactin level was never less than 100 nanog (ng)/ml. In Group C, the fasting prolactin level was less than 100 ng/ml in 6/13 patients. The prolactin increase following stimulation with thyrotropin releasing hormone (TRH) was 55 ng/ml (520%) in the control subjects (Group A) whereas in Groups B and C, the increase was less than 100%. It is suggested that the TRH test is the best method for determining whether a patient has a prolactinoma. A positive response to the TRH prolactin test does not necessarily rule out the possibility of a tumor, but a nonresponse of a hyperprolactinemic patient to TRH should be considered a definite indication of a prolactin microadenoma even in the absence of neuroradiologic confirmation. (14 Refs) (In FRE)

9. POST-THERAPEUTIC HORMONAL SURVEILLANCE OF SOMATOTROPIC ADENOMAS.

Schaison G

Service d'Endocrinologie, Hopital Biceta, 78, rue du General-Leclere, F 94270 Le Kremlin-Bicetre, France

Ann Med Interne (Paris); 133(1):38-41 1982

Following treatment of somatotropic adenomas, acromegaly should be monitored by various tests. Growth hormone levels with provoked hyperglycemia are not sufficient in affirming the cure of acromegaly. If the plasma level is less than 5 nanog/ml, a thyroid releasing hormone (TRH) test is required. If the TRH test is negative, a complete growth hormone test or an insulin like growth factor test is useful. All these tests are necessary in order to assess the usefulness of complementing cobalt therapy. (12 Refs) (In FRE)

10. GONADOTROPIC ADENOMAS.

Warnet A, Lubetzki J, Gueris J, Franchimont P, Mikol J, Dubois M, George B

Service de Medecine interne, Hopital Lariboisiere, 2, rue Ambroise-Pare, F 75010 Paris, France

Ann Med Interne (Paris); 133(1):26-28 1982

Three patients with gonadotropic adenomas (GA) underwent hormone and immunofluorescent testing to establish a profile of clinical responses of patients with GA. Two patients were men (21 and 41 yr old) with intracranial hypertension and bitemporal hemianopsia with optic atrophy. The third patient was a 61-yr-old woman with bitemporal hemianopsia with optic atrophy. In all three cases, the basal level of follicle stimulating hormone (FSH) was very elevated (21 to 50 nanog (ng)/ml compared with the normal value of 1.5 ng/ml). The response of FSH to multiple hormone stimulation was extremely high (2,550 and 1,350 ng/ml, normal 70 ng/ml) in the men, but the woman did not respond to this test. All patients demonstrated a prolonged response to luteinizing release hormone (CLRH). Luteinizing hormone was blocked in all three cases by the administration of testosterone or estradiol. Although the final diagnosis of the gonadotropic nature of an adenoma usually comes from in vitro studies, it is suggested that the existence of a large adenoma with pituitary deficits and hypersecretion of FSH is a decisive argument for a definite diagnosis. (19 Refs) (In FRE)

11. REDUCED 3H-DOPAMINE UPTAKE BY BLOOD PLATELETS IN PATIENTS WITH PROLACTIN-SECRETING PITUITARY ADENOMA.

Nicoletti I, Capodicasa E, Santeusanio F, Neuci GG, Brunetti P
Semeiotica Medica e Patologia Medica, Istituti di Clinica Medica, University Perugia, Perugia, Italy
Horm Metab Res; 14(6):310-312 1982

Uptake of 3H-Dopamine by blood platelets was found to be significantly reduced in eight patients with prolactin (PRL) secreting pituitary adenoma in comparison to normal subjects (27.91 +-5.01 nmol/10(11) platelets vs 73.42 +-4.99 nmol/10(11) platelets, p less than 0.001). Since platelet monoamine uptake seems to reflect brain monoaminergic activity, the reduction of dopamine uptake (DAU) in our hyperprolactinemic subjects suggests a defective dopaminergic neurotransmission in patients with PRL-secreting tumors. (Author abstract) (24 Refs)

12. HYPERPROLACTINAEMIA IN MALES WITH AND WITHOUT PITUITARY MACROADENOMAS.

Spark RF, Wills CA, O'Reilly G, Ransil BJ, Bergland R
Steroid Res. Lab., Beth Israel Hosp., 330 Brookline Ave., Boston, MA, 02215
Lancet; 2(8290):129-132 1982

To ascertain whether in hyperprolactinemic men pituitary macroadenomas represent the end stage of a disease process wherein the only early symptom is impotence, the features of 16 hyperprolactinemic men with radiological evidence of pituitary macroadenomas were compared with those of 10 hyperprolactinemic men without pituitary macroadenomas. All were impotent and 25 had low serum testosterone levels. The group with pituitary macroadenoma was older (48.1 vs 63.2 yr) and had tolerated impotence for longer (10.4 +-6.0 vs 4.5 +-2.1 yr). Six of them had visual field defects (none in the other group), 14 had hypopituitarism (1 in the other group), and 14 were initially seen for problems other than sexual dysfunction (whereas all 10 without pituitary macroadenomas were seen primarily for evaluation of recent onset of impotence). In the macroadenoma group bromocriptine restored serum prolactin levels in 13 of the 16 and serum testosterone and potency in 5, whereas in the nontumor group it restored serum prolactin levels in all 10 and serum testosterone and potency in 9. (Author abstract) (19 Refs)

13. INFLUENCE OF PREGNANCIES ON PROLACTINOMAS.

Rjosk HK, Fahlbusch R, Von Werder K
I. Frauenklinik der Universitat, Maistrasse 11, 8000 Munchen 2, W. Germany
Acta Endocrinol (Copenh); 100(3):337-346 1982

Hyperprolactinemic patients desiring pregnancy with a normal sella turcica or radiological evidence for a microprolactinoma without suprasellar extension were treated with bromocriptine. Females desiring pregnancy with large adenomas or suprasellar extension were treated by transsphenoidal surgery and in most instances post-operatively with bromocriptine. This differentiated management allowed the outcome of 65 pregnancies with delivery at term without complications related to the sella turcica. Considerable variations of prolactin levels during pregnancy suggesting different estrogen sensitivity of the prolactinoma cells were encountered. However, a rapid fall of the prolactin levels in 60 patients after termination of pregnancy indicated that estrogen stimulation does not cause persisting growth of the adenoma. In contrast, in 10% of pregnancies of hyperprolactinemic patients a reduction of the prolactin levels has been observed leading to spontaneous ovulatory cycles in five patients. (Author abstract) (22 Refs)

14. HYPOTHALAMO-PITUITARY FUNCTION IN FOUR CASES OF TRUE PRECOCIOUS PUBERTY.

Buonagnidi R, Ferdeghini M, Leoncini R, Tusini G

Istituto di Neurochirurgia dell'Universita, Spedali S. Chiara, via Roma 5, I-56100 Pisa, Italy

Childs Brain; 9(3/4):211-221 1982

Endocrinological data are presented for cases of true precocious puberty in three boys and one girl (6-9 yr old) before and after surgery for an astrocytoma of the anterior part of the third ventricle, involving the chiasm; an optic-chiasm glioma and a hydrocephalus secondary to aqueductal stenosis in the presence of neurofibromatosis; a third ventricle arachnoid cyst; and a postinfectious hydrocephalus. Computed tomography scans and serum gonadotropin levels after luteinizing hormone releasing hormone (LHRH) stimulation are discussed. In all cases compression and destruction of the hypothalamus occurred. Initially 3/4 patients had serum gonadotropin levels of postpubertal type, and the males had high levels of serum testosterone except for one boy who was receiving medroxyprogesterone acetate therapy. After surgery, and in one case radiotherapy, the serum gonadotropins basally, and especially after LHRH stimulation, were reduced. Quality of life and behavior of the children appeared satisfactory, and in cases in which epiphyseal closure had occurred height reached acceptable levels. (11 Refs)

15. SYLVIAN AQUEDUCT SYNDROME. CHRONOLOGY OF TUMORS IN THE PINEAL REGION WITH SPECIAL REFERENCE TO EARLY DIAGNOSIS.

Sakata E, Takahashi K

Dept. Neurotology, Saitama Medical Sch., 350-04 Saitama, Iruma, Moroyama, Hongo 38, Japan

Excerpta Med Int Congr Ser; 582:429-435 1982

Cases of 21 patients, 13 with pinealoma and 8 with tumors originating from the posterior part of the third ventricle, were examined neurologically, with neurotological tests, angiography, pneumoencephalography, and computerized tomography performed repeatedly. A representative case of a 22-yr-old woman is described in detail. Abnormal eye movements were examined and divided into four stages. Stage I involved transient nystagmoid eye movement toward the lower eyelid on upward gaze and fine upbeat nystagmus on convergence. Stage II involved paretic upbeat nystagmus on upward gaze, convergence nystagmus with the eyes covered in an upward position, and mild inhibition of upward optokinetic nystagmus. Stage III was characterized by dissociated upward gaze palsy, convergence of refractory nystagmus on convergence with upward gaze, moderate inhibition of upward optokinetic nystagmus, induced convergence nystagmus or retractory nystagmus by optokinetic stimulation, and abnormal light reflex. Stage IV exhibited Parinaud's sign, spontaneous convergence or retractory nystagmus, and total inhibition of upward optokinetic nystagmus. The shifts between stages may not be progressive; a shift to a lower stage is possible after therapy. Attention to subjective symptoms such as blurred vision and headaches and examination of ocular movements may allow early diagnosis of tumors manifesting Sylvian aqueduct syndrome. (12 Refs)

16. STROKE-LIKE ONSET OF PINEAL REGION TUMORS IN TWO CHILDREN.

Scarfo GB, Piane R, Mencattini G, Tomaccini D
Divisione di Neurochirurgia, Universita di Siena, Piazza Duomo, I-53100 Siena, Italy
Childs Brain; 9(3/4):274-279 1982

A boy and girl, both 8-yr-old, presented with sudden violent headache with meningism which suggested subarachnoid hemorrhage (SAH) which was confirmed by examination of the cerebrospinal fluid. Computed tomography showed tumors of the pineal region. In one patient SAH occurred three more times accompanied by rapid growth of the tumor and death in less than 3 yr. The other patient had no further SAH and after a shunt operation for triventricular hydrocephalus showed regression of neurological deficits and was in excellent health. (6 Refs)

17. PINEAL REGION TUMORS: ENDOCRINOLOGICAL ASPECTS.

Giovannelli G
Clinica Pediatrica, Universita di Parma, via A. Gramsci, I-43100 Parma, Italy
Childs Brain; 9(3/4):267-273 1982

Relationships between pineal tumors and diabetes insipidus, precocious puberty, neuro-ophthalmologic signs, and other diagnostic indicators are discussed. Evidence supporting the view that the pineal gland and the superior cervical ganglia constitute an integration center for hormonal and neural signals includes production of two antigonadal principles in response to environment, feedback control of pineal activity by reproductive hormones, the role of norepinephrine released from pineal nerve endings in pineal metabolism, and the role of substances other than sex steroids in modifying pineal function. Study of the hormonal effects strictly dependent upon pineal function is hampered by the lack of confirmed cases and the problem of correlating endocrine signs and neuro-ophthalmological abnormalities with histopathologic abnormalities. Diabetes insipidus is an important early clinical sign of pineal region tumors. It is important to distinguish diabetes insipidus of central origin (CID) from nephrogenic diabetes insipidus and psychogenic polydipsia. Both differential diagnoses can be made by tests involving vasopressin levels. Data of polyuria and/or polydipsia should never be underestimated, especially in the male child. Not only diabetes mellitus should be excluded, but CID as well; once a diagnosis of CID is established and the rare familial form excluded, a tumor of the pineal region should be considered. In the presence of CID a thorough and global endocrinological evaluation should be done to demonstrate adenopituitary deficiency, one of the early clinical signs of pineal region tumors. (13 Refs)

18. PINEAL TUMORS IN CHILDHOOD: EPIDEMIOLOGY, PATHOPHYSIOLOGY, AND SURGICAL APPROACHES.

Raimondi AJ, Tomita T
Northwestern Univ. Medical Sch., 303 East Chicago Ave., Chicago, IL, 60611
Childs Brain; 9(3/4):239-266 1982

Experience with 26 pineal tumors is described. Histologic types included: dysgerminoma, medulloblastoma, benign astrocytoma, medulloepithelioma, pineocytoma, teratoma, and others. Tumors were mainly in the third ventricle or quadrigeminal cistern, with some extending into the thalamus, midbrain, and other areas. Symptoms and signs were generally those expressive of hydrocephalus and included headache, vomiting/nausea, diplopia, papilledema, Parinaud's syndrome, and abducens palsy. Calcification was invariably present. Computerized transmission tomography (CTT) and angiography were particularly useful in diagnosis and in planning the surgery. Irradiation is highly recommended, with or without surgery, but full head and spinal cord treatment should be reserved for those children with positive cytology. CTT studies do not provide sufficient information for the surgeon on location and identification of specific venous cisterns and arterial systems, whereas cerebral angiography can provide this information. Surgical approaches may be parasagittal, suboccipital, supracerebellar, or occipital/transtentorial, depending upon the circumstances. Radiotherapy should be instituted upon finding in the cerebrospinal fluid (CSF) such markers as human chorionic gonadotropin, carcinoembryonic antigen and alpha-fetoprotein as indicators of germ cell tumors. Craniotomy and biopsy of pineal tumors are necessary when the CSF studies are negative. (28 Refs)

19. HYPERPROLACTINEMIA AS THE FIRST SYMPTOM OF CRANIOPHARYNGIOMA.

Maira G, Di Rocco C, Anile C, Roselli R
Inst. Neurosurgery, Catholic Univ., Largo Gemelli, I-00168 Rome, Italy
Childs Brain; 9(3/4):205-210 1982

Endocrinological patterns observed in four patients (all girls, 15-16 yr old) with hyperprolactinemic (HLP) syndrome where craniopharyngiomas were observed are described and related to different locations of pituitary-hypothalamic compression. The prolactin values observed in 126 patients treated for different sellar pathologies were analyzed and compared with the four HPL patients. PRL values were elevated before surgery in all four patients; values in two patients returned to normal after surgery and remained high or increased in the others. In the larger series of patients, high basal levels of PRL were found in all cases of histologically confirmed PRL-secreting adenomas, and in some other lesions of the sellar region, such as other types of pituitary adenomas, other tumors of the same region, and intrasellar arachnoid diverticula. One of the recognized causes of high basal levels of PRL is reduction of dopaminergic control on the normal PRL-secreting cells due to mechanical compression or invasion of the hypothalamus or pituitary stalk. Surgical removal established a normal hypothalamo-pituitary connection in one case, which exhibited normal PRL after surgery; malfunction in the pituitary stalk continued in one case despite total removal of the craniopharyngioma. (5 Refs)

20. HYPOPITUITARISM AFTER SURGERY FOR CRANIOPHARYNGIOMA.

Grant DB, Lyen K
Dept. Endocrinology, Hosp. for Sick Children, Great Ormond St., London WC1, England
Childs Brain; 9(3/4):201-204 1982

Endocrinological sequelae in 73 children operated upon for craniopharyngioma are described; results in children treated only by aspiration of the cyst of the tumor are compared with those undergoing direct removal of the lesion. Thirteen cases were treated by cyst aspiration followed by radiotherapy; 58 had partial or complete tumor resection, with either further surgery or radiotherapy for recurrence; and 2 young children with large tumors received no surgical treatment. Five of the 13 cases treated by aspiration died; 4 as a result of tumor recurrence and 1 due to 'coning' a few hr after aspiration. Thirty-six

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of the 58 children treated by tumor resection were alive at the time of reporting; 16 died; and 6 have been lost to follow-up. There was a very high incidence of endocrine deficits in the group treated by surgery. Fifteen children grew at a normal rate for at least a yr postoperatively, but now 32 children have required growth hormone therapy. Although many children initially treated by tumor resection required further surgery, only one died as a direct result of recurrence. Thirteen deaths were attributed to pituitary deficiency and 2 deaths were of unknown cause. In addition to the deaths, 11 patients required emergency treatment for hypopituitarism. Aggressive surgical management of craniopharyngioma seems to significantly reduce recurrence, but it is associated with a very high incidence of potentially life-threatening pituitary deficits. (4 Refs)

21. CRANIOPHARYNGIOMA.

Till K
Hosp. Sick Children, Great Ormond St., London, England
Childs Brain; 9(3/4):179-187 1982

Current accepted concepts in treatment of craniopharyngioma in children are reviewed, and several series of cases from personal experience and the literature are discussed. Different workers have disagreed on the value of total excision; while some were enthusiastic, others found palliative treatment to be adequate, with much less disablement. Radiotherapy has been reported successful in prolonging life in some series but not in others. The availability of computed tomography (CT) scan for planning the operative approach, coupled with the improvements and techniques and the availability of the operating microscope, makes total excision an attractive goal for many surgeons. Total excision seems to carry a better prognosis than partial excision followed by radiotherapy. While one recent series showed little differences between partial and total excision in terms of mortality during follow-up, there were four deaths in the total-excision group at 3, 4, 8, and 9 yr after operation due to suprarenal insufficiency, and unrecognized or inadequate treatment, with no tumor recurrence. Another series showed 11/116 patients dying due to pituitary deficiency, not tumor recurrence. The recurrence rate for radiotherapy was similar to that after total removal, and this technique should be used in most situations whenever failure of total removal is known. The decision on whether to attempt total removal or not can be made with the help of CT; some cases are easier to treat with two operations, with total removal ultimately being achieved months or years after sub-total removal was undertaken. (9 Refs)

22. PITUITARY ADENOMAS AND OTHER TUMORS: REVIEW IN PERSPECTIVE OF DIAGNOSIS AND TREATMENT.

Raiti S
Natl. Pituitary Agency, Univ. Maryland Sch. Medicine, Baltimore, MD, 21201
Childs Brain; 9(3/4):147-155 1982

Progress in neuroscience, particularly in the radioimmunoassay identification of anterior pituitary hormones, is reviewed, and approaches to management of pituitary tumors and other tumors are discussed. The first major advance was the discovery of radioimmunoassay for human growth hormone, thyroid-stimulating hormone (TSH) and follicle-stimulating hormone. Newer immunological techniques permitting definitive diagnosis of pituitary tumors were a second step. The third major advance in technology occurred in the area of radiological techniques, including tomography, which may be carried out in thin-section, multidirectional hypocycloidal techniques, and most recently the computerized axial tomography (CT) scan. Endocrinological manifestations often are part of the presenting signs of adenomas in childhood, along with local pressure effects. Pituitary surgery may destroy hormone-producing cells, hence it is essential to differentiate nonfunctioning tumors such as craniopharyngioma, astrocytoma, and aneurysms, or pseudotumors such as the empty sella syndrome, from functioning pituitary tumors. When follow-up demonstrates the necessity, growth hormone, TSH, and gonadotropin replacement therapy should be used. Growth hormone replacement aids in controlling hypoglycemia, a newly recognized problem of postoperative management. Pituitary hormone deficiency can be a complication of other tumors, such as medulloblastoma. (12 Refs)

THYROID TUMORS

23. ARE SCINTIGRAPHY AND ECHOGRAPHY OF THE THYROID SUPPLEMENTARY METHODS OF EXAMINATION?.

De Haas G, Zijderlaan Versulis E
Afdeling Nucleaire Geneeskunde en Echografie, Diakonissenhuis, Utrecht, The Netherlands
Ned Tijdschr Geneeskd; 126(9):365-371 1982

Thirty-three patients (30-74 yr old) with thyroid changes were subjected to scintigraphy with 99mTc pertechnetate and ultrasonography, and the findings were compaed with the histological ones. Scintigraphy revealed localized or diffuse, inhomogeneous radioactivity distribution in 10/33 patients, in whom ultrasonography showed solid processes with or without signs of degeneration. The microscopic examinations revealed colloid nodular (and adenomatous) goiter. Scintigraphy showed reduction or absence of radioactivity uptake locally (cold spot) or in the entire lobe in 19/33 patients. Ultrasonography showed solid process in 16/19 patients, in whom the histological examinations demonstrated carcinoma in 3/16 cases (1 anaplastic carcinoma and 2 follicular carcinomas), adenoma in 5/16, and colloid nodular (and adenomatous) goiter in 8/16, and complex processes in 3/19, which were demonstrated to be colloid nodular (and adenomatous) goiter histologically. Locally increased radioactivity uptake (hot spots) were demonstrated by scintigraphy in 4/33 patients. Ultrasonography showed solid processes in 3/4 cases, while the histological examination revealed adenoma in 2/3 and colloid nodular (and adenomatous) goiter in 1/3. The ultrasonography showed complex process in 1/4 cases, identified histologically as colloid nodular (and adenomatous) goiter. The findings indicate that ultrasonography failed to provide any specific additional information for hot and cold nodules. (11 Refs) (In DUT)

24. DIAGNOSTIC VALUE OF ECHOGRAPHY IN THE STUDY OF THYROID NODULES: ULTRASONOGRAPHIC AND HISTOLOGICAL DATA FOR 103 'COLD' THYROID NODULES.

Cimitan M, Bruno A; Pasquotti GP; Petrillo M; Spaziante R; Zecchin R
Ospedale Civile di Pordenone, Pordenone, Italy
Minerva Med; 73(27):1885-1889 1982

One hundred and three scintigraphically cold thyroid nodules were subjected to ultrasonographic and subsequent histological examinations. The histological examinations revealed carcinomas in 0/10 ultrasonographically cystic nodules, in 6/72 solid nodules, and 1/21 mixed cystic-solid nodules. No echographic abnormalities pathognomonic of malignancy were found in any of the 103 nodules. Malignant tumor (undifferentiated carcinoma involving adjacent blood vessels) was diagnosed before surgery in one case only. (12 Refs) (In ITA)

25. CANCER IN CYSTIC LESIONS OF THE THYROID.

Hammer M, Wortsman J, Folse R
(c/o Folse) Dept. Surgery, Southern Illinois Sch. Medicine, PO Box 3926, Springfield, IL, 62708
Arch Surg; 117(8):1020-1023 1982

We reviewed the records of 341 patients who underwent thyroidectomy for the suspicion of cancer between 1975 and 1980. Cancer of the thyroid was found in 14% of them. Although cysts of the thyroid (pathologic finding of a fluid-filled cavity greater than 1 cm in diameter) were encountered in 35% of the patients, cysts were similarly distributed among patients with benign conditions (27%) or with cancer (33%). Most of the thyroid cysts in patients with carcinoma measured 2 to 4 cm in diameter. The cancer was found within the cystic cavity. The cysts in patients with cancer appeared to originate from necrosis of the tumor. B-mode ultrasonography was not reliable in differentiating cystic and solid lesions. The demonstration of the cystic nature of a thyroid nodule does not rule out the diagnosis of cancer of the gland. (Author abstract) (17 Refs)

26. THE PARATHYROID RISK IN THYROIDECTOMIES.

Cannoni M, Pech A, Tiziano J, Thomassin J, Goubert J, Zanaret M, Abdul S
C.H.U. Timone, chemin de l'Armee d'Afrique, F 13385 Marseille, France
Ann Otolaryngol Chir Cervicofac; 99(6):237-244 1982

Of 1,188 thyroidectomies 98 (8.5%) were cancer cases, 471 (39.5%) were solitary cold nodules, 429 (36%) were polynodular goiters, 161 (13.5%) were hyperthyroiditis, and 27 (2.5%) were thyroiditis. No case of definitive hypoparathyrodism was found, although a few cases (1%) occurred following surgery for recurrent tumors. Of the 98 patients treated with total thyroidectomy and mediastinal recurrent laryngeal lymph node dissection, only 76 patients were followed. Definitive hypoparathyroidism occurred in 22.5% of the cases, and transitory hypoparathyroidism in 4%. Only 64% of the patients with malignant tumors had normal calcium levels. Improved postoperative results were achieved with identification of the parathyroids before the operation and preservation of the vascular supply to the parathyroids. Preservation of the two superior parathyroids along with their vascular (arterial) connections was often possible with malignant tumors of the thyroid. Preservation of the parathyroids led to a significant reduction in the number of definitive hypoparathyroid cases. (19 Refs) (In FRE)

27. MEDULLARY CARCINOMA OF THE THYROID.

Paches AI, Propp RM, Abdullin NA, Anokhin BM
Center for Oncology Res., USSR Acad. Medical Sciences, Moscow, USSR
Vopr Onkol; 28(5):77-82 1982

The paper deals with a study of 42 cases of medullary carcinoma which accounts for 12.6% of all forms of thyroid cancer. The female-to-male ratio was 1.3:1, mean age 45 yr. Medullary carcinoma occurs sporadically in cases of familial endocrine syndrome. A case of Sipple's syndrome is reported. Medullar carcinoma is a hormonally-active tumor which produces calcitonin, the latter serving as a tumor market for this carcinoma. Medullary carcinoma is characterized by bilateral involvement of the thyroid, which is more frequent in cases of familial disease, and a high rate of incidence of regional metastases (82.5%). Apart from clinical diagnostic means, the disease is chiefly identified cytologically and by calcitonin assays in blood plasma. It is mainly treated by surgery; 5-and 10-yr survival rates are 87.2 and 80%, respectively. (Author abstract) (16 Refs) (In RUS)

28. A CASE OF MULTIPLE ENDOCRINE NEOPLASIA TYPE II B: ENDOCRINOLOGICAL EVALUATION AND FAMILY SCREENING.

Imai Y, Fukase M, Tsutsumi M, Fukami T, Sakaguchi K, Furumoto M, Yoshimoto Y, Matsukura S, Fujita T
Third Div., Dept. Medicine, Kobe Univ. Sch. Medicine, Kusunoki-cho, Chuo-ku, Kobe 650, Japan
Endocrinol Jpn; 29(1):49-56 1982

Multiple endocrine neoplasia Type II b in a 27-yr-old woman is reported. The patient had a history of megacolon resulting from an intestinal neuroma, medullary carcinoma of the thyroid, neuroma of the tongue and lips, hypertrophic corneal nerve, and Marfanoid habitus. Clinical tests suggested pheochromocytoma. Screening of the patient's family detected two members with hypercalcitonemia. The reported case is apparently the first in Japan accompanied by familial hypercalitonemia. (25 Refs)

29. MALIGNANCIES AND EXPOSURE OF THE YOUNG TO IONIZING RADIATION.

Schull WJ, Kato H
Center for Demographic and Population Genetics, Univ. Texas Health Science Center at Houston, Houston, TX
Cancer Bull; 34(3):84-89 1982

Risk of radiation-related malignancies in individuals exposed in the first two decades of life in Hiroshima and Nagasaki is described. The relative risk of death due to leukemia in the 'heavily' exposed, particularly among those individuals exposed in the first decade of life, is much higher than the relative risk for exposures at subsequent ages. For the three most common radiation-related malignancies, cancers of breast, lung, and stomach, the absolute risk of death, for age-at-death specific groups, is higher the younger the age at the time of the bombing (ATB). Carcinoma of the thyroid was diagnosed during life more commonly in persons who were less than 20 yr of age ATB. The excess incidence of the malignancy/10(6) person-yr-risk/rad was 2.1, 2.3, 0.33, 0.28, and-0.07 for exposures at less than 10, 10-19, 20-34, 35-49, and 50 or more yr of age ATB, respectively. A study of 339 fatal and nonfatal malignancies among young survivors in the period 1950-1974 demonstrated that aside from the increased frequency, the distribution of malignant solid tumors differed little from that seen among individuals who were 20 yr of age or older when exposed. The diminished risk of radiation-related breast cancer among females exposed in the circum-menopausal years suggests that the endocrinologic status and possibly other factors may influence this specific risk. Whether the increased risk extends uniformly to all exposed individuals or whether there are especially vulnerable, 'high-risk' persons, is unknown. (26 Refs)

30. THYROID INJURY AND EFFECTS ON GROWTH AND DEVELOPMENT IN THE MARSHALLESE CHILDREN ACCIDENTALLY EXPOSED TO RADIOACTIVE FALLOUT.

Sutow WW, Conard RA, Thompson KH
(c/o Thompson) Biology Dept., Brookhaven Natl. Lab., Upton, NY
Cancer Bull; 34(3):90-96 1982

Late effects of fallout exposure on Marshallese people, focusing on the effects on the thyroid glands and growth and development of children, are discussed. Until approx 9 yr after exposure the health status of the exposed people did not appear to be significantly different from that of unexposed people. Examinations of newborns of exposed parents did not reveal any detectable abnormalities which might have been related to radiation exposure. The greatest incidence of thyroid nodularity has been noted in the high-dose Rongelap group, particularly in the children exposed at less than 10 yr of age. Among the exposed patients, the ratio of benign lesions to carcinoma appears to be greater in children than in adults. Preventive treatment with thyroid hormone was given to exposed Rongelap people in 1965 and to Ailingnae people in 1969. The pattern of growth and development of the individuals who were children (less than or equal to 18 yr old) on March 1, 1954, regularly followed in the Rongelap people, showed a consistent retardation of stature among boys exposed at less than 10 yr of age; the differences are statistically significant only between ages 9 and 16, apparently because of the administration of thyroid medication after 1963. Stature retardation in exposed girls occurred earlier, was less prominent and of shorter duration than among exposed boys. Osseous maturation among exposed boys was significantly retarded, particularly among boys aged 14-16 yr, compared with that in unexposed age peers. Retardation in osseous maturation among exposed girls occurred primarily among those exposed at less than 5 yr of age and to a very limited degree in those exposed at age 5-10 yr. Adult stature did not differ significantly among exposed and nonexposed individuals. (19 Refs)

PARATHYROID TUMORS

31. FAMILIAL HYPOCALCIURIC HYPERCALCEMIA: THE RELATION TO PRIMARY PARATHYROID HYPERPLASIA.

Marx SJ, Spiegel AM, Levine MA, Rizzoli RE, Lasker RD, Santora AC, Downs RW, Aurbach GD, Young J, Pallotta J, Garber JR, Flier J
NIH, Bldg. 10, Rm. 9-C-101, Bethesda, MD, 20205
N Engl J Med; 307(7):416-426 1982

Familial hypocalciuric hypercalcemia (FHH) is reviewed on the basis of studies of large families. FHH is an autosomal dominant characteristic. Expression of FHH is lifelong. The severity of symptoms varies and may be mild. In kindreds with FHH, hypercalcemic members more frequently show fatigue, weakness, mental problems, polydipsia, polyuria, arthralgia, and headache than normocalcemic members. Signs attributable to FHH are rare. Parathyroid surgery is generally unsatisfactory for treatment of FHH. Regulation of serum calcium in FHH is apparently different from that in typical primary hyperparathyroidism (TPH). Total concentration and the ionized fraction of serum calcium are similar in FHH and TPH. Approx 50% of patients with FHH also have increased serum magnesium concentrations. Renal function is well-maintained in FHH. Renal resorption of calcium apparently is regulated by factors other than parathyroid hormone. A high level of immunoreactive parathyroid hormone in the plasma, increased mass of the parathyroid gland, and severe primary hyperparathyroidism in neonates indicate that parathyroid dysfunction is an integral feature of FHH. Mild parathyroid hyperplasia is a consistent feature. Other hereditary causes of primary parathyroid hyperplasia include neonatal severe primary hyperparathyroidism and familial multiple endocrine neoplasia. The prevalence of FHH is unknown. Most patients require no active treatment, since the rate of morbidity is low. Indications for intervention include severe primary hyperparathyroidism in neonates, which may be life-threatening, and pancreatitis. FHH may result from dysfunction in a single metabolic pathway. (92 Refs)

ADRENAL TUMORS

32. ADRENAL IMAGING WITH 131I-ADOSTEROL (NCL-6-131I) BY DIVERGING AND PINHOLE METHODS. II. ANALYSIS OF ABNORMAL ADRENAL IMAGES.

Nakajo M

Dept. Radiology, Kagoshima Univ. Sch. Medicine, Kagoshima 890, Japan

Nippon Igaku Hoshasen Gakkai Zasshi; 42(2):160-187 1982

Adrenal patterns formed with the aid of a adrenal diverging and pinhole images using 131I-Adosterol were analyzed in 43 cases of various adrenal disorders (including 3 pheochromocytomas, 1 nonfunctioning adrenal adenoma, and 8 metastatic adrenal tumors), 4 adrenal adjacent tumors, and 1 arrhenoblastoma of the ovary. Accuracy of locating the adrenal tumor-bearing glands was 28/29 with pinhole images and 21/30 with diverging images in baseline conditions. Diagnostic accuracy was not good using adrenal high/low ratios. The pinhole method was recommended for adrenal imaging. (45 Refs)

33. SURGICAL TREATMENT OF PRIMARY ALDOSTERONISM: REPORT OF 120 CASES.

Zheng C, Zu B, Cheng Y

Ruijin Hosp., Shanghai Second Medical Coll., Shanghai, People's Republic of China

Zhonghua Miniao Waike Zazhi; 3(1):38-40 1982

During a 23-yr period, surgery was performed on 120 patients (62 males, 58 females) with aldosteronism. Among them, 103 (86%) had tumors of the adrenal cortex: 49 were on the left and 52 on the right, 1 had tumors on both sides, 1 had adenocarcinoma on the right. In 14 patients there was proliferation of adrenal cortex on both sides. Post-peritoneal air contrast picture showed tumors with 32% efficiency, whereas radioisotope scintiscan of the adrenal gland showed tumors with 82% efficiency. After surgery, one one-fifth of the patients still showed hypertension which was easily controlled with drugs. (no Refs) (In CHI)

34. PRIMARY HYPERALDOSTERONISM: DIFFERENTIATION BETWEEN ALDOSTERONE-PRODUCING ADENOMA AND IDIOPATHIC ADRENOCORTICAL HYPERPLASIA.

Wambach G, Helber A, Bonner G, Hummerich W, Konrads A, Meurer KA
Medizinische Universitats-Poliklinik, Medizinische Klinik Koln-Merheim, Ostmerheimer Str. 200, 5000 Koln 91, W. Germany
Dtsch Med Wochenschr; 107(24):923-927 1982

The regulation of aldosterone secretion by sodium restricted and enriched diet was assessed in 21 patients with primary aldosteronism for differentiation between unilateral aldosterone-producing adenoma and adrenocortical hyperplasia causing autonomous aldosterone hypersecretion. Compared to 10 patients with idiopathic adrenocortical hyperplasia, urinary aldosterone excretion after 4 days of sodium restricted diet was significantly higher in 11 patients with established adenoma (41.3 +-16.3 ug/24 hr vs 19.8 +-8.5 ug/24 hr; p less than 0.005). After 6 days of sodium loading these differences became even more obvious (35.3 +-14.0 ug/24 hr vs 12.7 +-3.7 ug/24 hr; p less than 0.0005). Sodium excretion did not influence aldosterone secretion in the adenoma group. In patients with hyperplasia both parameters showed a negative correlation (r =-0.522; p less than 0.001). Differentiation without overlap between both patient groups was achieved by comparison of the quotient of aldosterone excretion and serum potassium level during sodium enriched diet. (Author abstract) (20 Refs) (In GER)

35. ADRENAL TUMORS OR CHROMAFFIN TISSUE ASSOCIATED WITH STENOSIS OF THE RENAL ARTERY. REPORT OF 5 CASES.

Romero R, Caralps A, Sarrias X, Martinez-Amenos A, Rama H, Andreu J, Ocon J, Capdevila JM, Gil-Vernet JM
Ciudad Sanitaria, Hospital 'Principes de Espana', Barcelona, Spain
Rev Clin Esp; 164(5):347-349 1982

The association of adrenal tumor or chromaffin tissue with stenosis of the homolateral renal artery was diagnosed in five 25-61-yr-old men. The tumors included three pheochromocytomas, one Conn's adenoma and one adrenal myelolipoma. The mechanism of stenosis of renal artery associated with pheochromocytoma is discussed. The association of stenosis with the other tumors is probably a coincidence. (18 Refs) (In SPA)

36. PERSISTENT HYPERTENSION AFTER RESECTION OF A PHEOCHROMOCYTOMA.

Ludmerer KM, Kissane JM, Hammerman M, Levitt R, Clutter W, Meltzer V, Bobzein B, Cryer P
Dept. Internal Medicine, Washington Univ. Sch. Medicine, St. Louis, MO
Am J Med; 73(1):97-104 1982

A 23-yr-old white woman admitted for evaluation of persistent hypertension following removal of a left pheochromocytoma is discussed. A 24-hr urine collection showed 'elevated catecholamines', and computed tomography (CT) demonstrated a left adrenal mass. At exploratory laparotomy a left adrenal pheochromocytoma was removed. Blood pressure in the recovery room was 120/80 mm Hg, and it remained at that level for 1 wk, at which time it rose to 180/100 mm Hg. A repeat abdominal CT scan was unremarkable. Because of persistent hypertension accompanied by hypokalemia, the patient was further evaluated. Intermittent frontal headaches continued, but the patient denied palpitations or diaphoresis. Blood pressure on readmission was 200/140 mm Hg. CT scans of the abdomen showed a fullness of the right adrenal gland and a differential in kidney size, the left kidney being smaller than the right. Arteriography disclosed total occlusion of the artery supplying the left lower pole of the kidney, an irregular nephrogram on that side, and a uniform and slightly enlarged right adrenal gland without neovascularity. After all catecholamine samples had been obtained, the patient began receiving phenoxybenzamine. The blood pressure remained inadequately controlled, and propranolol, hydrochlorothiazide, and spironolactone were added. Orthostatic hypotension developed. At repeated laparotomy, left nephrectomy was performed and the right adrenal pheochromocytoma was removed. Final diagnosis was pheochromocytoma of the right adrenal gland, ligated left renal artery, and partial infarction of the left kidney. (34 Refs)

37. IMMUNOREACTIVE SOMATOSTATIN IN CATECHOLAMINE-PRODUCING EXTRA-ADRENAL PARAGANGLIOMA.

Saito H, Saito S, Sano T, Kagawa N, Hizawa K, Tatara K
Dept. Lab. Medicine, Sch. Medicine, Univ. Tokushima, 2-50 Kuramoto-Cho, Tokushima 770, Japan
Cancer; 50(3):560-565 1982

A patient with catecholamine-producing extra-adrenal paraganglioma was found to have a high concentration of immunoreactive somatostatin (IR-SRIF) in the peripheral blood plasma (47.0 pg/ml, normal; 13.3 +-5.3 pg/ml, mean +- SD). After removal of the tumor, the plasma SRIF level fell within normal range (8.7 pg/ml). In the resected tumor, a considerable amount of IR-SRIF (71.0 ng/g wet wt) was also detected and SRIF-positive tumor cells were demonstrated by the immunoperoxidase technique. Chromatographic analysis of an extract of the tumor showed the presence of two IR-SRIF components of large molecular size besides a component consistent with authentic tetradecapeptide SRIF (SRIF 14), and one of these had the same molecular size as octacosapeptide SRIF (SRIF 28). This seems to be the first report of a catecholamine-producing extra-adrenal paraganglioma that produces IR-SRIF with molecular heterogeneity. (Author abstract) (39 Refs)

PANCREAS TUMORS

38. PERCUTANEOUS TRANSHEPATIC VENOUS SAMPLING OF GASTRIN: VALUE IN SPORADIC AND FAMILIAL ISLET-CELL TUMORS AND G-CELL HYPERFUNCTION.

Glowniak JV, Shapiro B, Vinik AI, Glaser B, Thompson NW, Cho KJ
(c/o Vinik), Univ. Hosp., SACB 2226, Ann Arbor, MI, 48109
N Engl J Med; 307(5):293-297 1982

The value of transhepatic venous sampling was assessed in eight patients (6 women, 2 men; 23-59 yr old) by attempting to identify the origin of gastrin hypersecretion. Five patients had multiple endocrine neoplasia type I, two had single sporadic gastrinomas, and one had G-cell hyperfunction. In all cases studied, gastrin responses to secretin were abnormal; one patient had a borderline elevated response, but was subsequently shown to have G-cell hyperfunction. Patients with multiple endocrine neoplasia type I differed in the site of maximal gastrin concentration; two patients had high levels in veins draining the head of the pancreas, one exhibited diffuse hypergastrinemia, and various other locations were indicated in three others. Patients with solitary tumors differed in the locations of highest gastrin concentrations. In multiple endocrine neoplasia type I, transhepatic venous sampling is generally unhelpful in treatment because of the multiple sites of origin of gastrin hypersecretion. In sporadic tumors the technique may indicate that the tumor is localized, and may allow cure by surgical excision. In the patient with G-cell hypersecretion, transhepatic venous sampling localized hypersecretion to the antrum, suggesting appropriate surgery. (18 Refs)

39. METASTATIC PANCREATIC VIPOMA: A CASE REPORT OF CLINICAL RESPONSE FOLLOWING TREATMENT WITH CORTICOSTEROIDS AND ACTINOMYCIN D.

Fennelly JJ, Cantwell B, Fielding JF, FitzGerald O, Collins PG, Buchanan KD

(c/o Cantwell) Dept. Medical Oncology, St. Vincent's Hosp., Elm Park, Dublin 4, Ireland

Clin Oncol; 8(2):167-170 1982

Gut endocrine tumors are increasingly reported. We report a dramatic and prolonged remission following the use of corticosteroids and actinomycin D in a patient with a metastatic vipoma of the pancreas, and high circulating levels of vasoactive intestinal polypeptide. Response following the use of this combination of drugs in metastatic vipoma has not been reported. (Author abstract) (8 Refs)

OTHER TUMORS OF GLANDULAR TISSUES

40. THE CLINICAL SIGNIFICANCE OF ESTROGEN RECEPTORS ASSAY IN PRIMARY BREAST CANCER.

Heuson JC, Paridaens R, Andry G, Toma S, Sylvester R, Mattheiem WH, Leclercq G

Dept. Internal Medicine, Jules Bordet Inst., Bruxelles, Belgium

Acta Thermogr; 6(1-3):5-9 1981

The clinical significance of estrogen receptor assay as an estimate of the hormone dependence of primary breast cancers and of their potential for regression following various endocrine manipulations are discussed. In a 43-yr-old woman with tumor recurring 19 yr after complete remission of a poorly differentiated ductal carcinoma induced by bilateral oophorectomy and adrenalectomy, estrogen receptor assay was negative. This suggests that the recurrent tumor developed, possibly by cell selection, from a hormone-independent cell clone present in the initial lesion. Estrogen receptor positive cases will respond in about 50-60% of cases while the rate of response is only 5-10% in estrogen receptor negative cases. Estrogen receptor concentration was found to be closely related to the therapeutic response and proved superior in this regard to the distinction of estrogen receptor positive vs negative in a series of women with inoperable, recurrent or metastatic breast cancer. Estrogen receptor assay may be useful in defining patients who are likely to benefit from adjuvant endocrine therapy, and in post-menopausal women in the selection of an appropriate therapy. In a large series of patients followed up for a long period after mastectomy, estrogen receptor status was of no prognostic value as to the post-operative course of the disease. (9 Refs)

41. TAMOXIFEN THERAPY FOR PREMENOPAUSAL AND POSTMENOPAUSAL JAPANESE FEMALES WITH ADVANCED BREAST CANCER.

Yoshida M, Murai H, Miura S

Section of Breast Surgery, Aichi Cancer Center Hosp., Tashiro-cho, Chikusa-ku, Nagoya 464, Japan

Jpn J Clin Oncol; 12(1):57-63 1982

Clinical effects of tamoxifen (TMX) were studied in Japanese women (mean age 49.3 yr) with advanced breast cancer. The patients had recurrent cancer (70 cases) or inoperable advanced cancer. Twenty-six patients were premenopausal and 48 were postmenopausal. The TMX was administered initially at a dose of 10 mg, 2x/day; patients showing no response or who showed response and deteriorated later were given 40 mg/day. Six patients were given 40 mg/day from the start due to extremely severe subjective symptoms. According to the criteria of the International Union against Cancer, the response rate was 23/74, but according to the Aichi Cancer Center criteria, marked + moderate responses were observed in 32/74. The effective period for patients with marked response was greater than 13 mo, and their mean total dose was greater than 12,000 mg. No difference in response rate was observed among the different age groups. Marked + moderate response were observed in 14/26 patients with soft tissue cancer, in 2/10 with skeletal tissue cancer, and in 6/11 with visceral cancer. No severe side effects such as leukopenia, thrombocytopenia, and hypercalcemia were observed. Administration of 20 mg/day resulted in a marked + moderate response rate of 46.1%. TMX was effective in both pre- and postmenopausal patients. (15 Refs)

42. TAMOXIFEN, AMINOGLUTETHIMIDE AND DANAZOL: EFFECT OF THERAPY ON HORMONES IN POST-MENOPAUSAL PATIENTS WITH BREAST CANCER.

Coombes RC, Powles TJ, Rees LH, Ratcliffe WA, Nash AG, Henk M, Ford HT, Gazet JC, Neville AM

Ludwig Inst. Cancer Res. (London Branch), Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England

Br J Cancer; 46(1):30-34 1982

Gonadotrophins, estradiol, androstenedione, testosterone and dehydroepiandrosterone sulfate (DHAS) were measured sequentially in 72 patients with advanced breast cancer receiving endocrine therapy of various types. Tamoxifen significantly reduced gonadotrophins but did not effect other hormones. Danazol also reduced gonadotrophins. Aminoglutethimide (AGT) reduced estradiol and DHAS but had no effect on gonadotrophins. The effects of administering tamoxifen, AGT and danazol together (TAD) were therefore examined. This combination reduced gonadotrophins, estradiol and DHAS, but no further than tamoxifen and AGT alone. The degree and duration of hormone suppression were similar in both responders and non-responders to tamoxifen, AGT or TAD, though patients responding to AGT showed more complete suppression at the end of the course of treatment, perhaps because they were treated longer. On relapse, adequate gonadotrophin and steroid suppression was demonstrated in patients receiving tamoxifen and AGT, respectively. We conclude that (a) response to endocrine therapy is unlikely to be related to the degree of endocrine suppression produced by the therapy; (b) combination endocrine therapy does not further reduce serum-hormone concentrations and (c) relapse is unlikely to be due to escape from the hormone-inhibitory effects of endocrine agents. (Author abstract) (11 Refs)

43. THYROID DISEASE AND BREAST CANCER: FINDINGS IN A LARGE CASE-CONTROL STUDY.

Kalache A, Vessey MP, McPherson K
Univ. Dept. Community Medicine and General Practice, Radcliffe Infirmary, Oxford OX2 6HE, England
Br J Surg; 69(7):434-435 1982

The relationship between thyroid disease and breast cancer was examined in 1,176 women (16-50 yr old) with breast cancer and 1,176 age-matched controls. Overall 61 women with breast cancer and 70 control women gave a history of thyroid disease. The results indicated no association between a history of thyroid disease and breast cancer. (5 Refs)

44. NUCLEAR ANDROGEN RECEPTOR ASSAY IN BIOPSY-SIZE SPECIMENS OF HUMAN PROSTATIC TISSUE.

Blankenstein MA, Bolt-de Vries J, Foekens JA
Dept. Biochemistry, Rotterdam Radio-Therapeutic Inst., P. O. Box 5201, 3008 AE Rotterdam, The Netherlands
Prostate; 3(4):351-359 1932

The applicability of nuclear androgen receptors (NAR) assay to the biopsy-size specimens and the relationship between the presence of receptors and the response to endocrine therapy were studied in prostatic tissue samples from the patients with benign prostatic hyperplasia or prostatic cancer. Samples of 500, 100, 50, and 25 mg were homogenized, and the nuclear extracts were incubated with (3H)methyltrienolone. The NAR levels, on the av, did not depend upon the sample size. However, the intratissue variation coefficient increased when sample wt was less than 50 mg. The large variation in NAR levels observed in a 50-mg sample was associated with a nonhomogenous distribution of NAR over the prostatic tissue. The NAR levels did not depend upon the presence of molybdate in culture medium or upon the percentage of epithelium in the tissue. It was concluded that the assay can be used for prediction of the clinical response provided that multiple biopsies are analyzed. (14 Refs)

45. EFFECT OF DIET ON PLASMA AND URINARY HORMONES IN SOUTH AFRICAN BLACK MEN WITH PROSTATIC CANCER.

Hill P, Wynder EL, Garbaczewski L, Walker AR
Dept. Surgery, Medical Sch., Univ. Cape Town, Observatory 7925, Cape Town, South Africa
Cancer Res; 42(9):3864-3869 1982

Epidemiological evidence suggests that the incidence and death rate from prostatic cancer, an endocrine-associated disease, are related to environmental factors including diet. In this study, a comparison of serum and urinary levels of steroid hormones was carried out in healthy, elderly, rural South African black men on a vegetarian diet (a low-risk population), and a comparable group of men with prostatic cancer. In these prostatic cancer patients, plasma androgen levels decreased, while estrogen levels increased. Concomitantly, the androsterone:etiocholanolone ratio increased, and a greater proportion of estrogens was excreted as estriol. When transferred to a Western diet, plasma androgens showed a further decrease and a greater increase in estrone in prostatic cancer patients. In prostatic cancer patients, the total urinary androgen and estrogen levels were unaltered. However, in elderly healthy men, the Western diet decreased the excretion of estrogens and androgens. Thus, a Western diet supplemented the decrease in plasma androgens initially present in these patients. Evidence suggests that the decrease in plasma androgens increases the estrogen:androgen ratio, which may lead to hyperplasia of the prostatic ductal epithelia, a change enhanced by a Western diet. Changes in urinary steroid hormone levels in South African black patients comparable to those reported in white prostatic cancer patients indicate that hormonal changes must be related to several environmental factors, apart from diet. A simultaneous study of the steroid hormone composition of blood and prostatic fluid in this low-risk population is suggested. (Author abstract) (54 Refs)

46. INCREASED ANDROGENIC ACTIVITY IN WELL-DIFFERENTIATED ENDOMETRIAL ADENOCARCINOMA.

Grattarola R
Ottava Strada 32, 20090 Milano Sifelice, Italy
Gynecol Oncol; 14(1):40-48 1982

Well-differentiated adenocarcinoma of the endometrium was diagnosed in three patients with polycystic ovary syndrome (PCO) and in two long-term users of an oral contraceptive (ethinylestradiol plus dimethisterone), all five at premenopausal age (from 28 to 36 yr). These patients had high urinary testosterone. None underwent hysterectomy; the three with PCO were treated by wedge resection of the ovaries, and the two oral contraceptive users by simple curettage and discontinuation of oral contraception. The treatment was able to revert the endometrial pattern to normal as well as decrease the urinary level of testosterone. These patients were followed up for 3 to 10 yr since the hormonal study and none has so far had a recurrence. The testosterone excretion level was determined in an additional 26 patients with well-differentiated adenocarcinoma and in 14 with undifferentiated adenocarcinoma of the endometrium. It was found that the testosterone excretion level was significantly increased in patients with well-differentiated adenocarcinoma but not in patients with undifferentiated adenocarcinoma of the endometrium. (Author abstract) (18 Refs)

OTHER CLINICAL ASPECTS OF ENDOCRINE TUMORS

47. GROWTH AND HORMONAL STATUS OF CHILDREN TREATED FOR BRAIN TUMOURS.

Shalet SM
Dept. Endocrinology, Christie Hosp., Manchester, England
Childs Brain; 9(3/4):284-293 1982

Radiation-induced growth hormone (GH) deficiency, and hypopituitarism in children treated for brain tumors not directly involving the hypothalamic-pituitary axis are reviewed, and the site of radiation-induced damage and mechanism of GH deficiency causing growth retardation are discussed. Radiation has been associated with impaired GH response, but children having intact hypothalamic-pituitary function with brain tumors requiring either partial or complete neurosurgical removal showed no significant difference in GH response after treatment, suggesting that neither the mere presence of a tumor in the brain nor neurosurgery could account for the GH deficiency observed in irradiated patients. Studies of 20 adult patients who previously had received irradiation for brain tumors showed an unusual number with shorter than normal stature, and three had an elevated basal serum thyroid-stimulating hormone level; no other abnormality in anterior pituitary function was observed. The major site of damage is apparently the hypothalamus. GH is the first hormone to be affected by radiation-induced damage to the hypothalamic-pituitary region. In one study 12/13 irradiated children grew poorly in the first yr, but those with lowered GH secretion grew just as poorly as the others. Monitoring of growth after treatment, with appropriate supplemental human GH therapy is recommended for all children treated for a brain tumor. (27 Refs)

ECTOPIC HORMONE PRODUCTION BY NON-ENDOCRINE TUMORS

48. ECTOPIC PRODUCTION OF ACTH BY WILMS' TUMOR.

Pombo M, Alvez F, Varela-Cives R, Iglesias-Diz JL, Martinon F, Castro-Gago M, Pena J
Unit Pediatric Oncology and Growth, Departamento de Pediatrica, Hosp. General Galicia, Santiago de Compostela, Spain
Horm Res; 16(3):160-163 1982

The authors present the second documented case of Wilms' tumor associated with the ectopic ACTH syndrome. This is a 7 1/2-yr-old girl who, on examination at the time of admission, had the classical cushingoid appearance. A large hard mass was palpable in the right side of the abdomen. Hormonal assays were consistent with Cushing's syndrome; the serum ACTH levels were extremely high. After surgical removal of the mass, we suspected a Stage I Wilms' tumor; this was confirmed by histopathological studies. After surgery, the girl quickly lost her cushingoid appearance and weight excess. Postoperative serum ACTH levels were normal. Ectopic hormone syndromes associated with tumors in childhood are discussed as well as the possible mechanism involved in the ectopic production of ACTH. (Author abstract) (13 Refs)

SELECTED PRECLINICAL STUDIES OF ENDOCRINE CANCERS

49. RELATIONSHIPS BETWEEN STIMULATED PROLACTIN RELEASE FROM GH CELLS AND CYCLIC AMP DEGRADATION AND FORMATION.

Gautvik KM, Kriz M, Jahnsen T, Haug E, Hansson V
Fysiologisk Institutt, Universitetet i Oslo, Karl Johansgt. 47, Oslo 1, Norway
Mol Cell Endocrinol; 26(3):295-308 1982

The relationship between stimulated prolactin (PRL) release and formation and inactivation of cyclic AMP (cAMP) was studied in clonal strains (GH3 and GH4C1) of PRL producing rat-pituitary tumor cells (GH cells) after treatment with thyroliberin (TRH) and theophylline (TEP). The effect of TRH on adenyl cyclase activity in crude membrane fractions was investigated. Measurements of cAMP hydrolysis gave a non-linear Lineweaver-Burk plot. Changes in phosphodiesterase (PDE) activity caused by treatment with TRH and TEP were observed in the soluble fraction or in homogenates of cells. The enzymic activities in the soluble fraction and in the particulate fraction showed the same kinetics indicating the presence of identical or closely related cAMP PDEs. The maximal effect on PDE was observed at 30 nanomoles TRH. When TEP enhanced the release of PRL, the cells had increased cAMP concentrations and reduced cyclic nucleotide PDE activity. The effect of TRH on cAMP PDE was duplicated by treatment of the cells with high concentrations of cAMP. The effect of TRH on cAMP hydrolysis was dose-dependent, affecting the apparent maximal velocity of the enzyme rather than Km. Results indicated that TRH and TEP cause a rise in cellular concentrations of cAMP via different mechanisms. The highly positive correlation between PRL release and cellular cAMP concentrations support the notion that in GH cells, cAMP is a mediator of PRL release. (24 Refs)

50. CHARACTERIZATION OF SEROTONIN UPTAKE IN CULTURED PHEOCHROMOCYTOMA CELLS. COMPARISON WITH NOREPINEPHRINE UPTAKE.

Yoffe JR, Borchardt RT
(c/o Borchardt) Dept. Biochemistry, Smissman Laboratories, Univ. Kansas, 2095 Ave. A, West Campus, Lawrence, KS, 66045
Mol Pharmacol; 21(2):368-373 1982

PC-12 cells were studied to find out whether they have an active uptake mechanism for 5-hydroxytryptamine (5-HT). The [3H]5-HT uptake at 37 C was concentration-dependent and exhibited Michaelis-Menten type kinetics. In the absence of external sodium the active uptake was reduced by 43-53%. The velocity of [3H]norepinephrine (NE) uptake at 37 C was concentration-dependent and exhibited saturation kinetics. The apparent Km of [3H]5-HT uptake was 0.39 uM, which was very similar to that reported for serotonergic neurons and platelets. The ability of iodoacetamide (5 milliM, mM), and 2,4-dinitrophenol (1 mM) to block the accumulation of [3H]5-HT and [3H]NE uptake indicated that the uptake occurred by active transport processes. [3H]NE uptake was blocked by ouabain (1 mM), but [3H]5-HT uptake was not affected. As expected, desmethylimipramine was more effective at blocking [3H]NE than [3H]5-HT uptake. The uptake of [3H]NE appeared to be more structurally specific as it was selectively inhibited by NE, whereas the uptake of [3H]5-HT was equally inhibited by both NE and 5-HT. Considerable inhibition of [3H]thymidine incorporation was observed after 30 and 90 min incubation with 6-hydroxydopamine. Equal cytotoxic effect was observed after 90 min of incubation with 5,6-dihydroxytryptamine. Results indicated that PC-12 cells can accumulate 5-HT from external medium by a non-saturable diffusion process and by high-affinity transport process. (32 Refs)

51. EFFECTS OF A PROLACTIN- AND ADRENOCORTICOTROPIN-SECRETING TUMOR ON GONADOTROPIN LEVELS AND ACCESSORY SEX ORGAN WEIGHTS IN ADULT MALE RATS: A POSSIBLE ROLE OF THE ADRENALS.

Weber RF, Ooms MP, Vreeburg JT
(c/o Vreeburg) Dept. Endocrinology, Growth, and Reproduction, Erasmus Univ., P.O. Box 1738, Rotterdam 3000 DR, The Netherlands
Endocrinology; 111(2):412-417 1982

The presence of the transplantable PRL- and ACTH-secreting tumor 7315a in intact male rats resulted in very high serum PRL levels, decreased levels of LH and FSH, and reduced weights of testes and accessory sex organs. In gonadectomized rats bearing a small testosterone-filled capsule, the tumor inhibited the postcastration rise in gonadotropins and reduced the weights of the prostate and seminal vesicles. However, after adrenalectomy of intact or gonadectomized male rats bearing a small testosterone-filled capsule, inhibitory effects of the tumor on serum gonadotropin levels or on reproductive organ weights were totally absent. These results show that in adrenalectomized male rats, hyperprolactinemia in itself does not affect gonadotropin secretion and the androgenic action of testosterone. Rather, the tumor might exert a gonadotropin inhibitory action through elevated levels of PRL combined with progesterone, which is secreted by the ACTH-stimulated adrenal. (Author abstract) (27 Refs)

52. NEURON SPECIFIC ENOLASE (NSE) IMMUNOSTAINING: A USEFUL TOOL FOR THE LIGHT MICROSCOPICAL DETECTION OF ENDOCRINE CELL HYPERPLASIA IN ADULT RATS EXPOSED TO ASBESTOS.

Sheppard MN, Johnson NF, Cole GA, Bloom SR, Marangos PJ, Polak JM
(c/o Polak) Dept. Histochemistry, Royal Postgraduate Medical Sch., Hammersmith Hosp., DuCane Road, London, England
Histochemistry; 74(4):505-513 1982

An immunocytochemical technique was employed to detect endocrine cells at the light microscopical level with the use of antibodies to neuron specific enolase (NSE). The technique demonstrated marked endocrine cell hyperplasia in the lungs of adult SPF Wistar rats exposed to asbestos. Two groups of 6-wk-old or newborn rats were exposed to an atmosphere containing 10 mg/cubic meter of UICC (Union Internationale Contre le Cancer) chrysotile B asbestos fibers for 7 hr/day, 5 days/wk for 12 mo from birth or 6 wk of age. A third group of newborn rats was similarly exposed but for only 3 mo. In the rats rats exposed for 12 mo, the NSE immunostaining of sections revealed marked endocrine cell hyperplasia. There were extensive changes with prominent bronchiolar fibrosis and alveolar wall thickening. In rats exposed for 3 mo, only minimal changes were seen with dust-laden macrophages within bronchioles and alveoli. No such changes were seen in the lungs of control rats. Immunostaining of NSE can be used to demonstrate endocrine cell hyperplasia, which is characterized by the frequent presence of very large, irregular cell clusters in the lungs of rats exposed to asbestos for 12 mo. The lungs of control rats contained only single cells or small regular clusters but never large irregular clusters. While electron microscopy can detect endocrine cell hyperplasia, there is a large sampling error which is inherent in the technique. NSE immunostaining permits investigation of large blocks of tissue. (35 Refs)

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